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Access DB#

SEARCH REQUEST FORM

92990

Scientific and Technical Information Center

Requester's Full Name: Brian Kwon Examiner #: 78155 Date: 5/1/93
 Art Unit: 1614 Phone Number 30 8-5377 Serial Number: 10/956-28677
 Mail Box and Bldg/Room Location: 2004 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

 Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: use of inhibitors of soluble Epoxide hydrolase etc.
 Inventors (please provide full names): Wein et al

Earliest Priority Filing Date: 7/02

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Jan Delaval

Reference Librarian

Biotechnology & Chemical Library

CM1 1E07 703-308-4498

jan.delaval@uspto.gov

see abstract

- a method of inhibiting the polymerization of VSM

i) derivative of urea (e.g. COU) DCU) clin 5

ii) lipid alkoxyde (clin 7)

iii) diglydohexyl carbodiide (clin 8)

iv) phenyl glycidol (e.g. 5-4 hydroxyphenyl glycidol) clin 9

v) chalcane oxide (e.g. 4-phenylchalcane oxide,

4-fluorochalcane oxide)

furanose comprising

CIS - Epoxycyclohexanecarboxylic acid (clin 17)

STAFF USE ONLY

Searcher: Car

Searcher Phone #: 4458

Searcher Location: 51513

Date Searcher Picked Up: 5/5/93

Date Completed: 5/5/93

Searcher Prep & Review Time: 20

Clerical Prep Time: 25

Online Time: 25

Type of Search

NA Sequence (#) ✓

AA Sequence (#) ✓

Structure (#) ✓

Bibliographic ✓

Litigation ✓

Fulltext ✓

Patent Family ✓

Other ✓

Vendors and cost where applicable

STN ✓

Dialog ✓

Questel/Orbit ✓

Dr.Link ✓

Lexis/Nexis ✓

Sequence Systems ✓

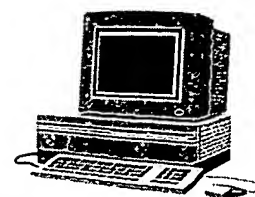
WWW/Internet ✓

Other (specify) ✓

BioTech-Chem Library

Search Results

Feedback Form (Optional)



Scientific & Technical Information Center

The search results generated for your recent request are attached. If you have any questions or comments (compliments or complaints) about the scope or the results of the search, please contact *the BioTech-Chem searcher* who conducted the search *or contact*:

Mary Hale, Supervisor, 308-4258
CM-1 Room 1E01

Voluntary Results Feedback Form

➤ *I am an examiner in Workgroup:* (Example: 1610)

➤ *Relevant prior art found, search results used as follows:*

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
(journal articles, conference proceedings, new product announcements etc.)

➤ *Relevant prior art not found:*

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Search results were not useful in determining patentability or understanding the invention.

Other Comments:

Drop off completed forms at the **Circulation Desk CM-1**, or send to **Mary Hale, CM1-1E01** or e-mail **mary.hale@uspto.gov**.

=> fil reg

FILE 'REGISTRY' ENTERED AT 17:36:10 ON 05 MAY 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 MAY 2003 HIGHEST RN 510703-80-7

DICTIONARY FILE UPDATES: 4 MAY 2003 HIGHEST RN 510703-80-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d ide.can

L88 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 57-13-6 REGISTRY

CN Urea (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN Aquacare

CN Aquadrate

CN B-I-K

CN Basodexan

CN Benural 70

CN Carbamide

CN Carbamimidic acid

CN Carbonyl diamide

CN Elaqua XX

CN Eucerin 10% Urea Lotion

CN Hyanit

CN Isourea

CN Keratinamin

CN Keratinamin Kowa

CN Nutraplus

CN Onychomal

CN Optigen 1200

CN Pastaron

CN Pastaron 10

CN Pastaron 20

CN Pastaron 20 soft

CN Pseudourea

CN UR

CN Urea perhydrate

CN Ureaphil

CN Ureophil

CN Urepeal

CN Urepeal L

CN Urepearl

CN Urevert

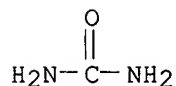
CN Varioform II

FS 3D CONCORD

DR 30535-50-3

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

MF C H4 N2 O
 CI COM
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS,
 BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB,
 CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU,
 DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2,
 ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB,
 IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PIRA,
 PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN,
 USPAT2, USPATFULL, VETU, VTB
 (*File contains numerically searchable property data)
 Other Sources: DSL**, EINECS**, TSCA**
 (**Enter CHEMLIST File for up-to-date regulatory information)



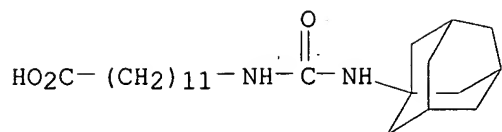
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

60370 REFERENCES IN FILE CA (1957 TO DATE)
 3020 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 60404 REFERENCES IN FILE CAPLUS (1957 TO DATE)
 9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:296786
 REFERENCE 2: 138:296597
 REFERENCE 3: 138:296368
 REFERENCE 4: 138:294819
 REFERENCE 5: 138:294582
 REFERENCE 6: 138:293383
 REFERENCE 7: 138:293022
 REFERENCE 8: 138:292840
 REFERENCE 9: 138:292784
 REFERENCE 10: 138:292745

=> d 161 ide can

L61 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2003 ACS
 RN 479413-70-2 REGISTRY
 CN Dodecanoic acid, 12-[[[(tricyclo[3.3.1.1³,7]dec-1-ylamino)carbonyl]amino]-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C23 H40 N2 O3
 SR CA
 LC STN Files: CA, CAPLUS



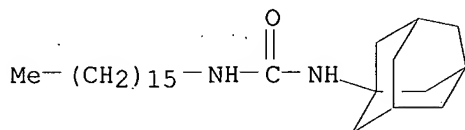
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REFERENCE 1: 138:49365

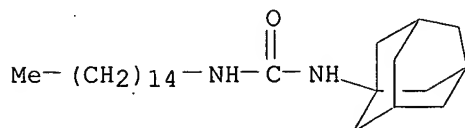
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L61 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2003 ACS
RN 327971-66-4 REGISTRY
CN Urea, N-hexadecyl-N'-tricyclo[3.3.1.13,7]dec-1-yl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H50 N2 O
SR Chemical Library
LC STN Files: CHEMCATS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L61 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2003 ACS
RN 120615-90-9 REGISTRY
CN Urea, N-pentadecyl-N'-tricyclo[3.3.1.13,7]dec-1-yl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H48 N2 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS

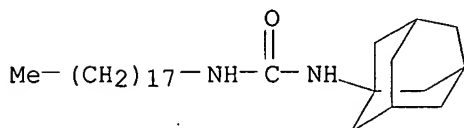


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 110:212200

L61 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2003 ACS
RN 73405-13-7 REGISTRY
CN Urea, N-octadecyl-N'-tricyclo[3.3.1.1.3,7]dec-1-yl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H54 N2 O
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

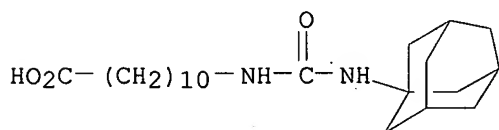


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 92:180710

L61 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2003 ACS
RN 33200-19-0 REGISTRY
CN Undecanoic acid, 1-[[[(tricyclo[3.3.1.1.3,7]dec-1-ylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Undecanoic acid, 11-[3-(1-adamantyl)ureido]- (8CI)
FS 3D CONCORD
MF C22 H38 N2 O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

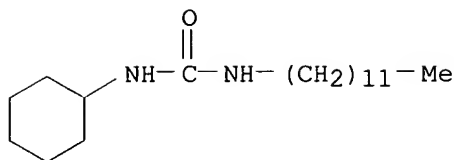
2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 78:71571

REFERENCE 2: 75:48734

=> d ide can 163

L63 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 402939-18-8 REGISTRY
CN Urea, N-cyclohexyl-N'-dodecyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C19 H38 N2 O
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1957 TO DATE)
4 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736

REFERENCE 2: 138:49365

REFERENCE 3: 137:88154

REFERENCE 4: 136:228661

=> d ide can 129

L29 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 2387-23-7 REGISTRY

CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Urea, 1,3-dicyclohexyl- (6CI, 7CI, 8CI)

OTHER NAMES:

CN 1,3-Dicyclohexylurea

CN Dicyclohexylcarbodiimide

CN N,N'-Dicyclohexylurea

FS 3D CONCORD

MF C13 H24 N2 O

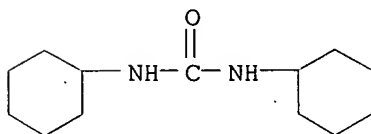
CI COM

LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MSDS-OHS, SPECINFO, SYNTHLINE, TOXCENTER, USPATFULL

(*File contains numerically searchable property data)

Other Sources: EINECS**, NDSL**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

339 REFERENCES IN FILE CA (1957 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
339 REFERENCES IN FILE CAPLUS (1957 TO DATE)
44 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:267583
 REFERENCE 2: 138:231736
 REFERENCE 3: 138:204645
 REFERENCE 4: 138:182942
 REFERENCE 5: 138:182263
 REFERENCE 6: 138:173298
 REFERENCE 7: 138:153330
 REFERENCE 8: 138:136558
 REFERENCE 9: 138:49365
 REFERENCE 10: 138:15240

=> d ide can 144

L44 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 538-75-0 REGISTRY

CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Carbodiimide, dicyclohexyl- (6CI, 7CI, 8CI)

OTHER NAMES:

CN 1,3-Dicyclohexylcarbodiimide

CN Bis(cyclohexyl)carbodiimide

CN DCC

CN DCCD

CN DCCI

CN Dicyclohexylcarbodiimide

CN N,N'-Dicyclohexylcarbodiimide

CN N,N'-Methanetetraylbis[cyclohexanamine]

FS 3D CONCORD

MF C13 H22 N2

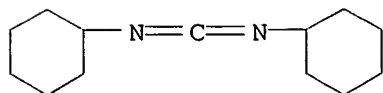
CI COM

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3245 REFERENCES IN FILE CA (1957 TO DATE)

65 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

3252 REFERENCES IN FILE CAPLUS (1957 TO DATE)

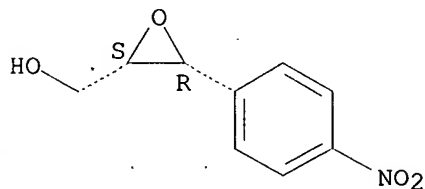
31 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:292417
REFERENCE 2: 138:290394
REFERENCE 3: 138:288241
REFERENCE 4: 138:287911
REFERENCE 5: 138:287249
REFERENCE 6: 138:271540
REFERENCE 7: 138:271246
REFERENCE 8: 138:267583
REFERENCE 9: 138:255621
REFERENCE 10: 138:255584

=> d ide can 149 tot

L49 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 143058-48-4 REGISTRY
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S-cis)- (9CI) (CA INDEX
NAME)
FS STEREOSEARCH
MF C9 H9 N O4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

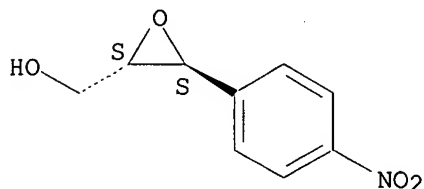
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 117:111338

L49 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 37141-34-7 REGISTRY
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)-rel- (9CI) (CA
INDEX NAME)
OTHER CA INDEX NAMES:
CN Oxiranemethanol, 3-(4-nitrophenyl)-, trans-(+-.)-
OTHER NAMES:
CN DL-trans-1-p-Nitrophenyl-1,2-epoxy-3-propanol
CN Oxiranemethanol, 3-(4-nitrophenyl)-, trans-
CN trans-1-p-Nitrophenyl-1,2-epoxy-3-propanol

CN trans-3-(4-Nitrophenyl)oxiranemethanol
FS STEREOSEARCH
DR 129830-80-4
MF C9 H9 N O4
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1957 TO DATE)
5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736
REFERENCE 2: 122:329493
REFERENCE 3: 78:71694
REFERENCE 4: 78:71663
REFERENCE 5: 77:61532

L49 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 37141-32-5 REGISTRY
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R-trans)-

OTHER NAMES:

CN (2R,3R)-(+)-3-(4-Nitrophenyl)glycidol

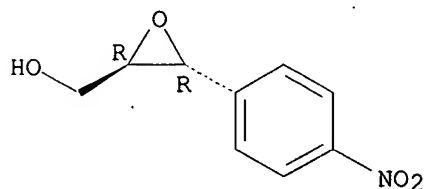
CN L-(+)-trans-1-p-Nitrophenyl-1,2-epoxy-3-propanol

FS STEREOSEARCH

MF C9 H9 N O4

LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, MSDS-OHS, RTECS*,
TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1957 TO DATE)
11 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736

REFERENCE 2: 134:42084

REFERENCE 3: 129:105945

REFERENCE 4: 122:329493

REFERENCE 5: 119:43970

REFERENCE 6: 119:8612

REFERENCE 7: 118:208242

REFERENCE 8: 117:2509

REFERENCE 9: 115:272840

REFERENCE 10: 78:71666

L49 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2003 ACS

RN 35587-52-1 REGISTRY

CN Oxiranemethanol, 3-(4-nitrophenyl)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1-Propanol, 2,3-epoxy-3-(p-nitrophenyl)- (6CI, 7CI)

OTHER NAMES:

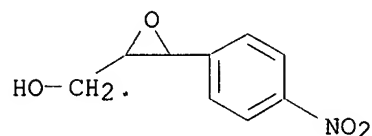
CN 1-(p-Nitrophenyl)-1,2-epoxy-3-propanol

FS 3D CONCORD

MF C9 H9 N O4

LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1957 TO DATE)

4 REFERENCES IN FILE CAPLUS (1957 TO DATE)

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 120:263215

REFERENCE 2: 115:46453

REFERENCE 3: 78:71662

REFERENCE 4: 76:126756

L49 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2003 ACS

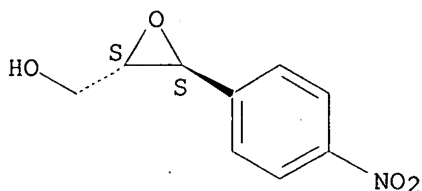
RN 1885-07-0 REGISTRY

CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1-Propanol, 2,3-epoxy-3-(p-nitrophenyl)-, trans-(-)- (8CI)
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S-trans)-
OTHER NAMES:
CN (2S,3S)-(-)-3-(4-Nitrophenyl)glycidol
CN D-(-)-trans-1-p-Nitrophenyl-1,2-epoxy-3-propanol
FS STEREOSEARCH
MF C9 H9 N O4
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, RTECS*, TOXCENTER,
USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



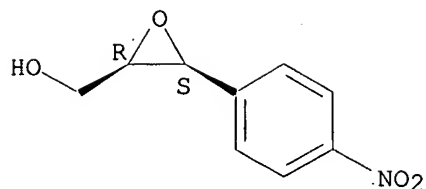
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14 REFERENCES IN FILE CA (1957 TO DATE)
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14 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736
REFERENCE 2: 136:102181
REFERENCE 3: 134:42084
REFERENCE 4: 129:105945
REFERENCE 5: 128:201056
REFERENCE 6: 122:329493
REFERENCE 7: 119:43970
REFERENCE 8: 118:208242
REFERENCE 9: 118:81235
REFERENCE 10: 117:2509

L49 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 1885-06-9 REGISTRY
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R-cis)- (9CI) (CA INDEX
NAME)
OTHER CA INDEX NAMES:
CN 1-Propanol, 2,3-epoxy-3-(p-nitrophenyl)-, cis-(+)- (8CI)
OTHER NAMES:
CN cis-(+)-3-(4-Nitrophenyl)oxiranemethanol
FS STEREOSEARCH
MF C9 H9 N O4
LC STN Files: BEILSTEIN*
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

=> d ide can 134

L34 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 5411-12-1 REGISTRY

CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Propiophenone, 2,3-epoxy-3-phenyl- (6CI, 7CI, 8CI)

OTHER NAMES:

CN 1,3-Diphenyl-2,3-epoxy-1-propanone

CN 1-Benzoyl-2-phenyloxirane

CN 2,3-Epoxy-1,3-diphenyl-1-propanone

CN 2,3-Epoxy-3-phenylpropiophenone

CN Chalcone epoxide

CN Chalcone oxide

CN Epoxybenzalacetophenone

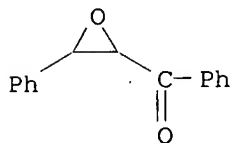
FS 3D CONCORD

MF C15 H12 O2

LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DETHERM*, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

154 REFERENCES IN FILE CA (1957 TO DATE)

4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

155 REFERENCES IN FILE CAPLUS (1957 TO DATE)

14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:237786

REFERENCE 2: 137:279032

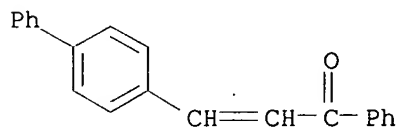
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REFERENCE 4: 136:38024

REFERENCE 5: 135:288644
REFERENCE 6: 134:178408
REFERENCE 7: 134:4819
REFERENCE 8: 133:277960
REFERENCE 9: 133:207753
REFERENCE 10: 133:89527

=> d ide can 135

L35 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 2403-28-3 REGISTRY
CN 2-Propen-1-one, 3-[1,1'-biphenyl]-4-yl-1-phenyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Chalcone, 4-phenyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 4-Phenylchalcone
FS 3D CONCORD
MF C21 H16 O
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, TOXCENTER,
USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

33 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
33 REFERENCES IN FILE CAPLUS (1957 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:116492
REFERENCE 2: 135:76687
REFERENCE 3: 129:256849
REFERENCE 4: 125:43887
REFERENCE 5: 120:149635
REFERENCE 6: 116:128292
REFERENCE 7: 112:155566
REFERENCE 8: 110:57712
REFERENCE 9: 104:201986

REFERENCE 10: 102:76014

=> d ide can 136

L36 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 1608-51-1 REGISTRY

CN 2-Propen-1-one, 3-(4-fluorophenyl)-1-phenyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Chalcone, 4-fluoro- (6CI, 7CI, 8CI)

OTHER NAMES:

CN 4-Fluorochalcone

CN p-Fluorostyryl phenyl ketone

CN Phenyl p-fluorostyryl ketone

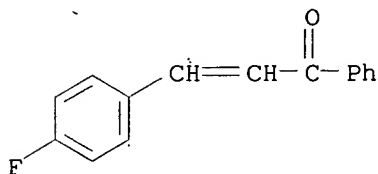
FS 3D CONCORD

MF C15 H11 F O

CI COM

LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS,
CHEMINFORMRX, HODOC*, IFICDB, IFIPAT, IFIUDB, SPECINFO, TOXCENTER,
USPATFULL

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

68 REFERENCES IN FILE CA (1957 TO DATE)

68 REFERENCES IN FILE CAPLUS (1957 TO DATE)

5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:262774

REFERENCE 2: 137:228474

REFERENCE 3: 136:332664

REFERENCE 4: 135:268889

REFERENCE 5: 134:366632

REFERENCE 6: 134:193210

REFERENCE 7: 133:249544

REFERENCE 8: 133:217539

REFERENCE 9: 133:207753

REFERENCE 10: 133:89124

=> d ide can 171

L71 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 97717-69-6 REGISTRY

CN Eicosatrienoic acid, epoxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Epoxyeicosatrienoic acid
MF C20 H32 O3
CI IDS
SR CA
LC STN Files: BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, TOXCENTER, USPAT2,
USPATFULL

CM 1

CRN 97717-68-5
CMF C20 H38 O3
CCI IDS

HO₂C-(CH₂)₁₈-Me

D1-O-D1

95 REFERENCES IN FILE CA (1957 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
95 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736
REFERENCE 2: 138:199178
REFERENCE 3: 138:150826
REFERENCE 4: 138:70306
REFERENCE 5: 137:349565
REFERENCE 6: 137:198627
REFERENCE 7: 137:120467
REFERENCE 8: 137:28024
REFERENCE 9: 136:338693
REFERENCE 10: 136:272910

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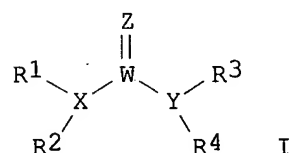
FILE COVERS 1907 - 5 May 2003 VOL 138 ISS 19
FILE LAST UPDATED: 4 May 2003 (20030504/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 190

L90 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN 2003:197917 HCAPLUS
DN 138:231736
TI Inhibitors of **epoxide hydrolases** for the treatment of hypertension
IN Kroetz, Deanna L.; Zeldin, Darryl C.; Hammock, Bruce D.; Morisseau, Christophe
PA Regents of the University of California, USA
SO U.S., 36 pp., Cont.-in-part of U.S. 6,150,415.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-335
NCL 514475000; 514529000; 514551000; 514625000; 514613000; 514631000; 514596000; 514588000; 514595000
CC 1-8 (Pharmacology)
Section cross-reference(s): 7, 14, 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6531506	B1	20030311	US 2000-721261	20001121
	US 5955496	A	19990921	US 1997-909523	19970812
	US 6150415	A	20001121	US 1999-252148	19990218
PRAI	US 1996-23397P	P	19960813		
	US 1997-909523	A2	19970812		
	US 1999-252148	A2	19990218		
OS	MARPAT 138:231736				
GI					



AB The invention provides compds. that inhibit **epoxide hydrolase** in therapeutic applications for the treatment of hypertension. A preferred class of compds. for practicing the invention have the structure shown by Formula [(R1)(R2)XW(Z)Y(R3)(R4)], wherein Z is oxygen or sulfur, W is carbon phosphorous or sulfur, X and Y is each independently nitrogen, oxygen, or sulfur, and X can further be carbon, at least one of R1-R4 is hydrogen, R2 is hydrogen when X is nitrogen but is not present when X is sulfur or oxygen, R4 is hydrogen when Y is nitrogen but is not present when Y is sulfur or oxygen, R1 and R3 is each independently C1-C20 substituted or unsubstituted alkyl, cycloalkyl, aryl, acyl, or heterocyclic.

ST **epoxide hydrolase** inhibitor antihypertensive design
human pregnancy hypertension

IT Pregnancy

(-induced hypertension; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Enzyme functional sites
(active; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Kidney
(cortex; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Antihypertensives
Drug design
Human
Hypertension
Kidney
Microsome
Mouse
Rat
Urine
(**epoxide hydrolases** inhibitors for treatment of hypertension)

IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxide hydrolases** inhibitors for treatment of hypertension)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunoreactive; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Diagnosis
(of hypertension or risk for hypertension; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Drug delivery systems
(oral; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT 60-33-3, Linoleic acid, biological studies 9048-63-9,
Epoxide hydrolase 97717-69-6,
Epoxyeicosatrienoic acid 192461-94-2 192461-95-3 192461-96-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxide hydrolases** inhibitors for treatment of hypertension)

IT 101-20-2 538-75-0 886-59-9 1142-07-0 1145-53-5 1220-01-5
1885-07-0 2222-58-4 2387-23-7 3218-00-6 4300-43-0
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501011-71-8				

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(epoxide hydrolases inhibitors for treatment of
hypertension)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 9048-63-9, **Epoxide hydrolase**
 97717-69-6, **Epoxyeicosatrienoic acid**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (**epoxide hydrolases** inhibitors for treatment of hypertension)
 RN 9048-63-9 HCAPLUS
 CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 97717-69-6 HCAPLUS
 CN Eicosatrienoic acid, epoxy- (9CI) (CA INDEX NAME)

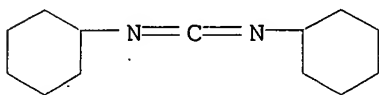
CM 1

CRN 97717-68-5
 CMF C20 H38 O3
 CCI IDS

HO₂C- (CH₂)₁₈-Me

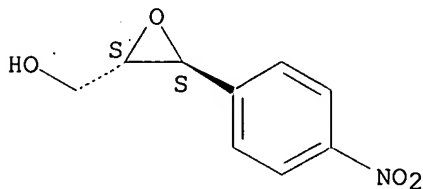
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IT 538-75-0 1885-07-0 2387-23-7
 37141-32-5 37141-34-7 402939-18-8
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (**epoxide hydrolases** inhibitors for treatment of hypertension)
 RN 538-75-0 HCAPLUS
 CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)

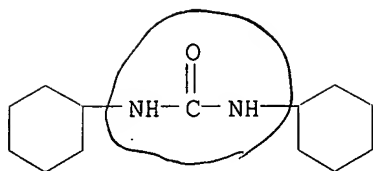


RN 1885-07-0 HCAPLUS
 CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



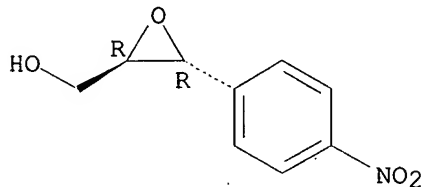
RN 2387-23-7 HCAPLUS
 CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



RN 37141-32-5 HCAPLUS

CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

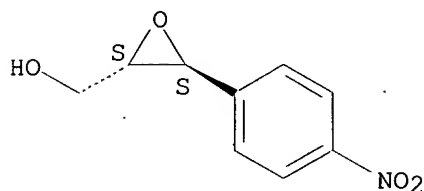
Absolute stereochemistry.



RN 37141-34-7 HCAPLUS

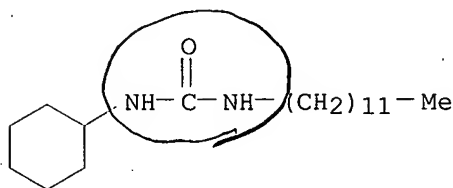
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 402939-18-8 HCAPLUS

CN Urea, N-cyclohexyl-N'-dodecyl- (9CI) (CA INDEX NAME)



L90 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:854210 HCAPLUS

DN 138:267583

TI Urea and amide-based inhibitors of the juvenile hormone **epoxide hydrolase** of the tobacco hornworm (*Manduca sexta*: Sphingidae)AU Severson, Tonya F.; Goodrow, Marvin H.; Morisseau, Christophe; Dowdy, Deanna L.; **Hammock, Bruce D.**

CS Department of Entomology and Cancer Research Center, University of California, Davis, CA, 95616, USA

SO Insect Biochemistry and Molecular Biology (2002), 32(12), 1741-1756
CODEN: IBMBES; ISSN: 0965-1748

PB Elsevier Science Ltd.

DT Journal

LA English

CC 7-3 (Enzymes)

Section cross-reference(s): 12

- AB A new class of inhibitors of juvenile hormone **epoxide hydrolase** (JHEH) of *Manduca sexta* and further in vitro characterization of the enzyme are reported. The compds. are based on urea and amide pharmacophores that were previously demonstrated as effective inhibitors of mammalian sol. and microsomal **epoxide hydrolases**. The best inhibitors against JHEH activity so far within this class are N-[(Z)-9-octadecenyl]-N'-propylurea and N-hexadecyl-N'-propylurea, which inhibited hydrolysis of a surrogate substrate (t-DPPO) with an IC50 around 90 nM. The importance of substitution no. and type was investigated and results indicated that N, N'-disubstitution with asym. alkyl groups was favored. Potencies of pharmacophores decreased as follows: amide>urea>carbamate>carbodiimide>thiourea and thiocarbamate for N,N'-disubstituted compds. with sym. substituents, and urea>amide>carbamate for compds. with asym. N,N'-substituents. JHEH hydrolyzes t-DPPO with a Km of 65.6 .mu.M and a Vmax of 59 nmol min-1 mg-1 and has a substantially lower Km of 3.6 .mu.M and higher Vmax of 322 nmol min-1 mg-1 for JH III. Although none of these compds. were potent inhibitors of hydrolysis of JH III by JHEH, they are the first leads toward inhibitors of JHEH that are not potentially subject to metab. through epoxide degrdn.
- ST juvenile hormone **epoxide hydrolase** inhibitor tobacco hornworm *Manduca*
- IT Structure-activity relationship
(enzyme-inhibiting; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (*Manduca sexta*))
- IT Juvenile hormones
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(kinetic parameters; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (*Manduca sexta*))
- IT Optical refraction
(molar refraction, of juvenile hormones; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (*Manduca sexta*))
- IT Enzyme kinetics
(of inhibition; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (*Manduca sexta*))
- IT *Manduca sexta*
Michaelis constant
(urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (*Manduca sexta*))
- IT 57-13-6, Urea, biological studies 102-07-8, 1,3-Diphenylurea 111-26-2, 1-Hexanamine 111-68-2, 1-Heptanamine 112-20-9, 1-Nonanamine 112-90-3, cis-9-Octadecenylamine 124-22-1, 1-Dodecanamine 124-30-1, 1-Octadecanamine 143-27-1, 1-Hexadecanamine 301-02-0, Oleamide 538-75-0 598-94-7, N,N-Dimethylurea 623-95-0, 1,3-Dipropylurea 632-22-4, Tetramethylurea 698-90-8, Cyclohexylurea 886-59-9, 1-Cyclohexyl-3-phenylurea 1212-29-9 2016-57-1, 1-Decanamine 2158-09-0, Dodecylurea 2387-23-7, 1,3-Dicyclohexylurea 2869-34-3, 1-Tridecanamine 3359-39-5 7307-55-3, 1-Undecanamine 20258-07-5 25855-24-7 31510-11-9 55398-22-6 70243-17-3 72802-45-0 72802-46-1 118389-04-1 128276-09-5, 1-Octyl-3-propylurea 147642-79-3 158072-24-3 246165-77-5 246165-79-7 347907-04-4 348594-28-5 392713-22-3 460745-85-1 479413-19-9 500346-45-2 501003-81-2 501003-96-9 501003-98-1 503114-33-8 503114-39-4 503114-40-7 503114-42-9 503114-43-0 503114-44-1 503114-45-2 503114-46-3 503114-47-4 503114-48-5 503114-49-6 503114-50-9 503114-51-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitor; urea and amide-based inhibitors of juvenile hormone
epoxide hydrolase of tobacco hornworm (*Manduca sexta*))

IT 5255-04-9 21213-74-1 23314-84-3

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(juvenile hormone; urea and amide-based inhibitors of juvenile hormone
epoxide hydrolase of tobacco hornworm (*Manduca sexta*))

IT 65095-03-6

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(substrate, kinetic parameters; urea and amide-based inhibitors of
juvenile hormone **epoxide hydrolase** of tobacco
hornworm (*Manduca sexta*))

IT 69106-46-3P, Juvenile hormone **epoxide hydrolase**

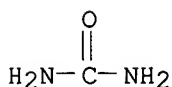
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
BIOL (Biological study); PREP (Preparation)
(urea and amide-based inhibitors of juvenile hormone **epoxide
hydrolase** of tobacco hornworm (*Manduca sexta*))

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

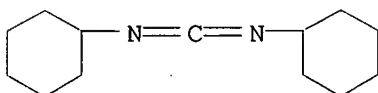
RE

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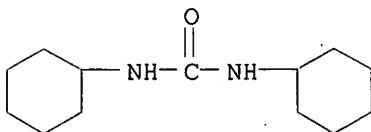
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 IT 57-13-6, Urea, biological studies 538-75-0
 2387-23-7, 1,3-Dicyclohexylurea
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitor; urea and amide-based inhibitors of juvenile hormone
 epoxide hydrolase of tobacco hornworm (Manduca
 sexta))
 RN 57-13-6 HCAPLUS
 CN Urea (8CI, 9CI) (CA INDEX NAME)



RN 538-75-0 HCAPLUS
 CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)



RN 2387-23-7 HCAPLUS
 CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



L90 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2003 ACS
 AN 2002:340739 HCAPLUS
 DN 138:49365
 TI Structural refinement of inhibitors of urea-based soluble **epoxide hydrolases**
 AU Morisseau, Christophe; Goodrow, Marvin H.; Newman, John W.; Wheelock, Craig E.; Dowdy, Deanna L.; Hammock, Bruce D.
 CS Department of Entomology, University of California, Davis, CA, 95616, USA
 SO Biochemical Pharmacology (2002), 63(9), 1599-1608
 CODEN: BCPA6; ISSN: 0006-2952
 PB Elsevier Science Inc.
 DT Journal
 LA English
 CC 1-3 (Pharmacology)
 AB The sol. **epoxide hydrolase** (sEH) is involved in the metab. of arachidonic, linoleic, and other fatty acid epoxides, endogenous chem. mediators that play an important role in blood pressure regulation and inflammation. 1,3-Disubstituted ureas, carbamates, and amides are new potent and stable inhibitors of sEH. However, the poor soly. of the lead compds. limits their use. Inhibitor structure-activity relationships were investigated to better define the structural requirements for inhibition and to identify points in the mol. topog. that could accept polar groups without diminishing inhibition potency. Results indicate that

lipophilicity is an important factor controlling inhibitor potency. Polar groups could be incorporated into one of the alkyl groups without loss of activity if they were placed at a sufficient distance from the urea function. The resulting compds. had a 2-fold higher water soly. These findings will facilitate the rational design and optimization of sEH inhibitors with better phys. properties.

ST urea inhibitor prepn structure activity lipophilicity **epoxide**

hydrolase

IT Blood pressure

Crystal structure

Drug design

Human

Lipophilicity

Mouse

Solubility

Structure-activity relationship

(structural refinement of inhibitors of urea-based sol. **epoxide**

hydrolases)

IT 9048-63-9, **Epoxide hydrolase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(structural refinement of inhibitors of urea-based sol. **epoxide**

hydrolases)

IT 2387-23-7 287185-29-9

RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)

(structural refinement of inhibitors of urea-based sol. **epoxide**

hydrolases)

IT 886-59-9P 1145-53-5P 1220-01-5P 2222-58-4P 13074-28-7P
 17427-95-1P 29559-44-2P 38652-23-2P 62972-70-7P 72802-46-1P
 75461-45-9P 89609-46-1P 108195-84-2P 120615-85-2P 124949-24-2P
 148806-87-5P 179539-07-2P 195451-88-8P 200058-85-1P 200059-00-3P
 201349-42-0P 401589-91-1P **402939-18-8P** 479412-88-9P
 479412-91-4P 479413-00-8P 479413-14-4P 479413-19-9P 479413-36-0P
 479413-39-3P 479413-45-1P 479413-50-8P 479413-53-1P 479413-55-3P
 479413-57-5P 479413-59-7P 479413-61-1P 479413-63-3P 479413-65-5P
 479413-68-8P **479413-70-2P**

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(structural refinement of inhibitors of urea-based sol. **epoxide**

hydrolases)

IT 124-22-1, Dodecylamine 3173-53-3, Cyclohexyl isocyanate 5452-37-9, Cyclooctylamine

RL: RCT (Reactant); RACT (Reactant or reagent)

(structural refinement of inhibitors of urea-based sol. **epoxide**

hydrolases)

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IT 9048-63-9, **Epoxide hydrolase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)

RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

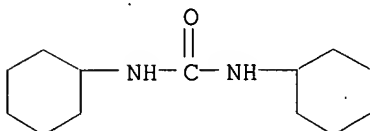
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IT 2387-23-7

RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
 (structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)

RN 2387-23-7 HCAPLUS

CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)

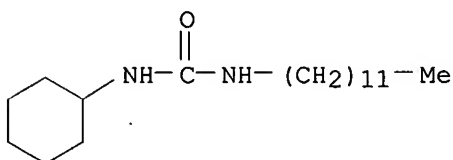


IT 402939-18-8P 479413-70-2P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)

RN 402939-18-8 HCAPLUS

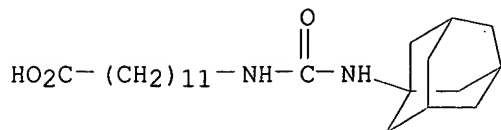
CN Urea, N-cyclohexyl-N'-dodecyl- (9CI) (CA INDEX NAME)



RN 479413-70-2 HCAPLUS

CN Dodecanoic acid, 12-[[((tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)carbonyl)amino]-

(9CI) (CA INDEX NAME)



L90 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2003 ACS
 AN 2002:200865 HCAPLUS
 DN 137:88154
 TI Inhibitors of soluble **epoxide hydrolase** attenuate
 vascular smooth muscle cell proliferation
 AU Davis, Benjamin B.; Thompson, David A.; Howard, Laura L.; Morisseau,
 Christophe; **Hammock, Bruce D.; Weiss, Robert H.**
 CS Division of Nephrology, Department of Internal Medicine, Cell and
 Developmental Biology Graduate Group, University of California, Davis, CA,
 95616, USA
 SO Proceedings of the National Academy of Sciences of the United States of
 America (2002), 99(4), 2222-2227
 CODEN: PNASA6; ISSN: 0027-8424
 PB National Academy of Sciences
 DT Journal
 LA English
 CC 1-8 (Pharmacology)
 Section cross-reference(s): 14
 AB Atherosclerosis, in its myriad incarnations the foremost killer disease in
 the industrialized world, is characterized by aberrant proliferation of
 vascular smooth muscle (VSM) cells in part as a result of the recruitment
 of inflammatory cells to the blood vessel wall. The
epoxyeicosatrienoic acids are synthesized from arachidonic acid in
 a reaction catalyzed by the cytochrome P 450 system and are vasoactive
 substances. Metab. of these compds. by **epoxide**
hydrolases results in the formation of compds. that affect the
 vasculature in a pleiotropic manner. As an outgrowth of our observations
 that urea inhibitors of the sol. **epoxide hydrolase**
 (sEH) reduce blood pressure in spontaneously hypertensive rats as well as
 the findings of other investigators that these compds. possess
 antiinflammatory actions, we have examd. the effect of sEH inhibitors on
 VSM cell proliferation. We now show that the sEH inhibitor 1-
cyclohexyl-3-dodecyl urea (CDU) inhibits human
 VSM cell proliferation in a dose-dependent manner and is assocd. with a
 decrease in the level of cyclin D1. In addn., **cis-**
epoxyeicosatrienoic acid mimics the growth-suppressive activity of
 CDU; there is no evidence of cellular toxicity or apoptosis in CDU-treated
 cells when incubated with 20 .mu.M CDU for up to 48 h. These results, in
 light of the antiinflammatory and antihypertensive properties of these
 compds. that have been demonstrated already, suggest that the urea class
 of sEH inhibitors may be useful for therapy for diseases such as
 hypertension and atherosclerosis characterized by exuberant VSM cell
 proliferation and vascular inflammation.
 ST **epoxyeicosatrienoate** CDU antiatherosclerotic antihypertensive
 antiinflammatory signaling; antihypertensive **epoxide**
hydrolase inhibitor apoptosis metab **epoxyeicosatrienoic**
 acid
 IT Cyclins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (D1; inhibitors of sol. **epoxide hydrolase** attenuate
 vascular smooth muscle cell proliferation)
 IT Antiarteriosclerotics

- (antiatherosclerotics; inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)
- IT Anti-inflammatory agents
 Antihypertensives
 Apoptosis
 Atherosclerosis
 Cardiovascular agents
 Human
 Signal transduction, biological
 (inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)
- IT Blood vessel
 (smooth muscle; inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)
- IT Hypertension
 (spontaneous; inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)
- IT 9035-51-2, Cytochrome P 450, biological studies 9048-63-9, **Epoxide hydrolase** 142243-02-5, MAP kinase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)
- IT 80558-45-8D, epoxides 402939-18-8
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)

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IT 9048-63-9, **Epoxide hydrolase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors of sol. **epoxide hydrolase** attenuate
 vascular smooth muscle cell proliferation)

RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

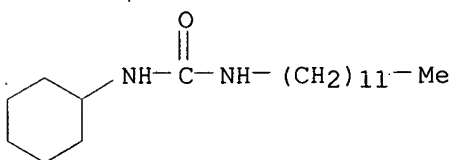
IT 402939-18-8

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT
 (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)

(inhibitors of sol. **epoxide hydrolase** attenuate
 vascular smooth muscle cell proliferation)

RN 402939-18-8 HCAPLUS

CN Urea, N-cyclohexyl-N'-dodecyl- (9CI) (CA INDEX NAME)



L90 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:161988 HCAPLUS

DN 136:338693

TI Soluble **epoxide hydrolase** inhibition lowers arterial
 blood pressure in angiotensin II hypertension

AU Imig, John D.; Zhao, Xueying; Capdevila, Jorge H.; Morisseau, Christophe;
 Hammock, Bruce D.

CS Vascular Biology Center, Department of Physiology, Medical College of
 Georgia, Augusta, GA, USA

SO Hypertension (2002), 39(2, Pt. 2), 690-694
 CODEN: HPRTDN; ISSN: 0194-911X

PB Lippincott Williams & Wilkins

DT Journal

LA English

CC 14-5 (Mammalian Pathological Biochemistry)
 Section cross-reference(s): 1

AB **Epoxyeicosatrienoic** acids (EETs) have antihypertensive
 properties and play a part in the maintenance of renal microvascular
 function. A novel approach to increase EET levels is to inhibit
epoxide hydrolase enzymes that are responsible for
 conversion of biol. active EETs to dihydroxyeicosatrienoic acids (DHETs)
 that are void of effects on the preglomerular vasculature. We
 hypothesized that inhibition of sol. **epoxide hydrolase**
 (sEH) would lower blood pressure in angiotensin II (Ang II) hypertension.
 Rat renal cortical tissue was harvested and urine collected 2 wk following
 implantation of an osmotic minipump contg. Ang II (60 ng/min). Renal
 cortical sEH protein expression was significantly higher in Ang II
 hypertension compared with normotensive animals. Likewise, urinary
 14,15-DHET levels were significantly increased in hypertensive compared

with normotensive animals and averaged 8.1 ± 1.3 and 2.7 ± 1.1 ng/d; resp. In addnl. expts., the sEH inhibitor N-cyclohexyl-N-dodecyl urea (NCND; 3 mg/d) or vehicle (corn oil, 0.5 mL) was administered daily by i.p. injection starting on day 10. Administration of NCND for 4 days lowered systolic blood pressure by 30 mm Hg in Ang II hypertensive animals, whereas the corn oil vehicle had no effect on blood pressure in normotensive or Ang II hypertensive animals. Measurement of blood pressure by indwelling arterial catheters in conscious animals with free movement in their cages confirmed that NCND had antihypertensive properties. Arterial blood pressure averaged 119 ± 5 mm Hg in normotensive, 170 ± 3 mm Hg in hypertensive and 149 ± 10 mm Hg in NCND-treated, Ang II-infused animals. Administration of the potential metabolite of NCND, N-cyclohexylformamide to Ang II hypertensive rats did not lower the systolic blood pressure. These studies demonstrate that increased sEH expression in the Ang II hypertensive kidney leads to increased EET hydration. Moreover, sEH plays a role in the regulation of blood pressure, and inhibition of sEH during Ang II hypertension is antihypertensive.

- ST **epoxide hydrolase** blood pressure angiotensin II hypertension; **epoxyeicosatrienoate** hydration dihydroxyeicosatrienoate urine **epoxide hydrolase** antihypertensive
- IT Hydration, physiological
(increased renal sol. **epoxide hydrolase** leads to increased **epoxyeicosatrienoic** acid hydration in angiotensin II hypertension)
- IT Kidney
Urine
(kidney sol. **epoxide hydrolase** levels are elevated in angiotensin II hypertension and assocd. with increased levels of urinary 14,15-dihydroxyeicosatrienoic acid)
- IT Antihypertensives
Blood pressure
Hypertension
(sol. **epoxide hydrolase** inhibition in lowering arterial blood pressure in angiotensin II hypertension)
- IT 97717-69-6, **Epoxyeicosatrienoic** acid
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increased renal sol. **epoxide hydrolase** leads to increased **epoxyeicosatrienoic** acid hydration in angiotensin II hypertension)
- IT 79551-81-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(kidney sol. **epoxide hydrolase** levels are elevated in angiotensin II hypertension and assocd. with increased levels of urinary 14,15-dihydroxyeicosatrienoic acid)
- IT 11128-99-7, Angiotensin-II
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(sol. **epoxide hydrolase** inhibition in lowering arterial blood pressure in angiotensin II hypertension)
- IT 9048-63-9, **Epoxide hydrolase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sol.; sol. **epoxide hydrolase** inhibition in lowering arterial blood pressure in angiotensin II hypertension)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT 97717-69-6, **Epoxyeicosatrienoic acid**

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(increased renal sol. **epoxide hydrolase** leads to increased **epoxyeicosatrienoic acid** hydration in angiotensin II hypertension)

RN 97717-69-6 HCAPLUS

CN Eicosatrienoic acid, epoxy- (9CI) (CA INDEX NAME)

CM 1

CRN 97717-68-5

CMF C20 H38 O3

CCI IDS

HO₂C-(CH₂)₁₈-Me

D1-O-D1

IT 9048-63-9, **Epoxide hydrolase**

RL: BSU (Biological study, unclassified); BIOL (Biological study) (sol.; sol. **epoxide hydrolase** inhibition in lowering arterial blood pressure in angiotensin II hypertension)

RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:863088 HCAPLUS

DN 136:116492

TI Leukotoxin-Diol. A putative toxic mediator involved in acute respiratory distress syndrome

AU Zheng, Jiang; Plopper, Charles G.; Lakritz, Jeffery; Storms, David H.;
Hammock, Bruce D.

CS Department of Pharmaceutical Sciences, School of Pharmacy, Bouve College
of Health Sciences, Northeastern University, Boston, MA, 02115, USA

SO American Journal of Respiratory Cell and Molecular Biology (2001), 25(4),
434-438
CODEN: AJRBEL; ISSN: 1044-1549

PB American Thoracic Society

DT Journal

LA English

CC 14-4 (Mammalian Pathological Biochemistry)

AB Leukotoxin is clin. assocd. with acute respiratory distress syndrome
(ARDS). Recently, we found that leukotoxin-diol, the hydrated product of
leukotoxin, is more toxic than the parent leukotoxin in vitro. To test if
this difference in the toxicity of leukotoxin and leukotoxin-diol exists
in vivo, Swiss Webster mice were administered leukotoxin or
leukotoxin-diol. All mice treated with leukotoxin-diol died of ARDS-like
respiratory distress, whereas the animals exposed to leukotoxin at the
same dose survived. Histopathol. evaluation of the lungs revealed massive
alveolar edema and hemorrhage with interstitial edema around blood vessels
in the lungs of mice treated with leukotoxin-diol, whereas the lungs of
mice treated with identical doses of leukotoxin had perivascular edema
only and little change in alveolar spaces. Immunohistochem. showed that
the sol. **epoxide hydrolase** responsible for the
hydrolysis of leukotoxin to its diol is concd. in the vascular smooth
muscle of small and medium-sized pulmonary vessels. In addn., 4
-phenylchalcone oxide, an inhibitor of sol.
epoxide hydrolase, was found to decrease the mortality
induced by leukotoxin but had no effect on mortality induced by
leukotoxin-diol. These studies provide strong in vivo evidence that
leukotoxin may act as a protoxicant and that the corresponding diol is a
putative toxic mediator involved in the development of ARDS.

ST leukotoxin diol toxic mediator respiration distress syndrome

IT Respiratory distress syndrome
(acute; leukotoxin-diol. a putative toxic mediator involved in acute
respiratory distress syndrome in mice)

IT Lung
(alveolus; leukotoxin-diol. a putative toxic mediator involved in acute
respiratory distress syndrome in mice)

IT Hydrolysis
(biol.; leukotoxin-diol. a putative toxic mediator involved in acute
respiratory distress syndrome in mice)

IT Lung, disease
(injury; leukotoxin-diol. a putative toxic mediator involved in acute
respiratory distress syndrome in mice)

IT Edema
Hemorrhage
(leukotoxin-diol. a putative toxic mediator involved in acute
respiratory distress syndrome in mice)

IT Toxins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(leukotoxins; leukotoxin-diol. a putative toxic mediator involved in
acute respiratory distress syndrome in mice)

IT Blood vessel
(smooth muscle; leukotoxin-diol. a putative toxic mediator involved in
acute respiratory distress syndrome in mice)

IT 189191-41-1, Leukotoxin-Diol
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(leukotoxin-diol. a putative toxic mediator involved in acute
respiratory distress syndrome in mice)

IT 2403-28-3D, 4-Phenylchalcone, oxide
9048-63-9, Epoxide hydrolase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
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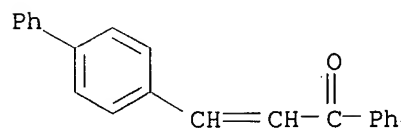
IT 2403-28-3D, 4-Phenylchalcone, oxide

9048-63-9, Epoxide hydrolase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

RN 2403-28-3 HCAPLUS

CN 2-Propen-1-one, 3-[1,1'-biphenyl]-4-yl-1-phenyl- (9CI) (CA INDEX NAME)



RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:367801 HCAPLUS

DN 135:135057

TI Pathways of **epoxyeicosatrienoic** acid metabolism in endothelial cells. Implications for the vascular effects of soluble **epoxide hydrolase** inhibition

AU Fang, Xiang; Kaduce, Terry L.; Weintraub, Neal L.; Harmon, Shawn; Teesch, Lynn M.; Morisseau, Christophe; Thompson, David A.; **Hammock, Bruce D.**; Spector, Arthur A.

CS Department of Biochemistry, College of Medicine, University of Iowa, Iowa City, IA, 52242, USA

SO Journal of Biological Chemistry (2001), 276(18), 14867-14874
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 13-2 (Mammalian Biochemistry)

AB **Epoxyeicosatrienoic** acids (EETs) are products of cytochrome P 450 epoxigenase that possess important vasodilating and anti-inflammatory properties. EETs are converted to the corresponding dihydroxyeicosatrienoic acid (DHET) by sol. **epoxide hydrolase** (sEH) in mammalian tissues, and inhibition of sEH has

been proposed as a novel approach for the treatment of hypertension. The authors obsd. that sEH is present in porcine coronary endothelial cells (PCEC), and the authors found that low concns. of N,N'-dicyclohexylurea (DCU), a selective sEH inhibitor, have profound effects on EET metab. in PCEC cultures.— Treatment with 3 .mu.M DCU reduced cellular conversion of 14,15-EET to 14,15-DHET by 3-fold after 4 h of incubation, with a concomitant increase in the formation of the novel .beta.-oxidn. products 10,11-epoxy-16:2 and 8,9-epoxy-14:1. DCU also markedly enhanced the incorporation of 14,15-EET and its metabolites into PCEC lipids. The most abundant product in DCU-treated cells was 16,17-epoxy-22:3, the elongation product of 14,15-EET. Another novel metabolite, 14,15-epoxy-20:2, was present in DCU-treated cells. DCU also caused a 4-fold increase in release of 14,15-EET when the cells were stimulated with a calcium ionophore. Furthermore, DCU decreased the conversion of [3H]11,12-EET to 11,12-DHET, increased 11,12-EET retention in PCEC lipids, and produced an accumulation of the partial .beta.-oxidn. product 7,8-epoxy-16:2 in the medium. These findings suggest that in addn. to being metabolized by sEH, EETs are substrates for .beta.-oxidn. and chain elongation in endothelial cells and that there is considerable interaction among the three pathways. The modulation of EET metab. by DCU provides novel insight into the mechanisms by which pharmacol. or mol. inhibition of sEH effectively treats hypertension.

- ST **epoxyeicosatrienoic acid metab epoxide**
hydrolase oxidn coronary endothelium pig
- IT Artery
(coronary, endothelium; pathways of **epoxyeicosatrienoic acid** metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT Blood vessel
(endothelium; pathways of **epoxyeicosatrienoic acid** metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT Antihypertensives
(pathways of **epoxyeicosatrienoic acid** metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphoinositides
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pathways of **epoxyeicosatrienoic acid** metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT Oxidation
(.beta.-; pathways of **epoxyeicosatrienoic acid** metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT 26764-25-0, Octadecadienoic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(epoxy derivs.; pathways of **epoxyeicosatrienoic acid** metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT 506-32-1, Arachidonic acid 197508-62-6
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

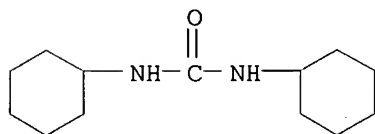
- (pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT 9048-63-9, **Epoxide hydrolase**
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT 7440-70-2, Calcium, biological studies 200960-01-6
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT 192461-94-2 192461-95-3 261967-98-0 261968-00-7 261968-01-8
 351533-79-4 351533-80-7 351533-81-8
 RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
- IT 2387-23-7, N,N'-Dicyclohexylurea
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

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 IT 9048-63-9, **Epoxide hydrolase**
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
 RN 9048-63-9 HCAPLUS
 CN Hydratase, epoxide (9CI) (CA INDEX NAME)
- *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 IT 2387-23-7, N,N'-Dicyclohexylurea
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
 RN 2387-23-7 HCAPLUS
 CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



- L90 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2003 ACS
 AN 2000:878331 HCAPLUS
 DN 134:54845
 TI Soluble **epoxide hydrolase** regulates hydrolysis of vasoactive **epoxyeicosatrienoic** acids
 AU Yu, Zhigang; Xu, Fengyun; Huse, Linn M.; Morisseau, Christophe; Draper, Alison J.; Newman, John W.; Parker, Carol; Graham, LeRae; Engler, Marguerite M.; Hammock, Bruce D.; Zeldin, Darryl C.; Kroetz, Deanna L.
 CS Department of Biopharmaceutical Sciences, School of Nursing, University of California, San Francisco, CA, USA
 SO Circulation Research (2000), 87(11), 992-998
 CODEN: CIRUAL; ISSN: 0009-7330
 PB Lippincott Williams & Wilkins
 DT Journal
 LA English
 CC 14-5 (Mammalian Pathological Biochemistry)
 AB The cytochrome P 450-derived **epoxyeicosatrienoic** acids (EETs) have potent effects on renal vascular reactivity and tubular sodium and

water transport; however, the role of these eicosanoids in the pathogenesis of hypertension is controversial. The current study examined the hydrolysis of the EETs to the corresponding dihydroxyeicosatrienoic acids (DHETs) as a mechanism for regulation of EET activity and blood pressure. EET hydrolysis was increased 5- to 54-fold in renal cortical S9 fractions from the spontaneously hypertensive rat (SHR) relative to the normotensive Wistar-Kyoto (WKY) rat. This increase was most significant for the 14,15-EET regioisomer, and there was a clear preference for hydrolysis of 14,15-EET over the 8,9- and 11,12-EETs. Increased EET hydrolysis was consistent with increased expression of sol.

epoxide hydrolase (sEH) in the SHR renal microsomes and cytosol relative to the WKY samples. The urinary excretion of 14,15-DHET was 2.6-fold higher in the SHR than in the WKY rat, confirming increased EET hydrolysis in the SHR in vivo. Blood pressure was decreased 22 mm Hg 6 h after treatment of SHRs with the selective sEH inhibitor N,N'-**dicyclohexylurea**; this treatment had no effect on blood pressure in the WKY rat. These studies identify sEH as a novel therapeutic target for control of blood pressure. The identification of a potent and selective inhibitor of EET hydrolysis will be invaluable in sepg. the vascular effects of the EET and DHET eicosanoids.

- ST **epoxide hydrolase** kidney **epoxyeicosatrienoate**
hydrolysis blood pressure; hypertension eicosanoid metab **epoxide hydrolase** kidney
- IT Kidney
(cortex; sol. **epoxide hydrolase** of kidney
regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)
- IT Cytoplasm
(cytosol; sol. **epoxide hydrolase** of kidney
regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)
- IT Antihypertensives
(sol. **epoxide hydrolase** inhibitors decrease of
blood pressure in hypertension)
- IT Blood pressure
(sol. **epoxide hydrolase** of kidney regulation of
hydrolysis of vasoactive **epoxyeicosatrienoic** acids in blood
pressure regulation)
- IT Microsome
Urine
(sol. **epoxide hydrolase** of kidney regulation of
hydrolysis of vasoactive **epoxyeicosatrienoic** acids in
hypertension)
- IT Eicosanoids
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
BSU (Biological study, unclassified); BIOL (Biological study); PROC
(Process)
(sol. **epoxide hydrolase** of kidney regulation of
hydrolysis of vasoactive **epoxyeicosatrienoic** acids in
hypertension)
- IT Hypertension
(spontaneous; sol. **epoxide hydrolase** of kidney
regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)
- IT 2387-23-7, N,N'-Dicyclohexylurea
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sol. **epoxide hydrolase** inhibitor decrease of blood
pressure in hypertension)
- IT 81246-85-7 81276-02-0 81276-03-1
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
BSU (Biological study, unclassified); BIOL (Biological study); PROC

(Process)

(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT 79551-81-8 97717-67-4

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT 9048-63-9, **Epoxide hydrolase**

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT 97717-69-6, **Epoxyeicosatrienoic acid**

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(triunsatd.; sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

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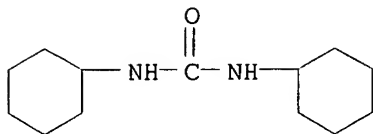
IT 2387-23-7, **N,N'-Dicyclohexylurea**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sol. **epoxide hydrolase** inhibitor decrease of blood pressure in hypertension)

RN 2387-23-7 HCAPLUS

CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



IT 9048-63-9, **Epoxide hydrolase**

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process) (sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 97717-69-6, **Epoxyeicosatrienoic acid**

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (triunsatd.; sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

RN 97717-69-6 HCAPLUS

CN Eicosatrienoic acid, epoxy- (9CI) (CA INDEX NAME)

CM 1

CRN 97717-68-5

CMF C20 H38 O3

CCI IDS

HO₂C- (CH₂)₁₈-Me

D1-O-D1

L90 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 2000:821596 HCAPLUS

DN 133:349972

TI Preparation of ureas and related compounds as soluble **epoxide hydrolase** inhibitors.

IN Hammock, Bruce D.; Morisseau, Christophe H.; Zheng, Jiang; Goodrow, Marvin H.; Severson, Tonya; Sanborn, James

PA The Regents of the University of California, USA

SO U.S., 17 pp., Cont.-in-part of U. S. 5,955,496.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-17

NCL 514588000

CC 23-20 (Aliphatic Compounds)

Section cross-reference(s): 1, 5

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US_6150415	A	20001121	US 1999-252148	19990218
	US 5955496	A	19990921	US 1997-909523	19970812
	US 6174695	B1	20010116	US 1999-312207	19990514
	EP 1154764	A1	20011121	EP 2000-911767	20000210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT; IE, SI, LT, LV, FI, RO				
	JP 2002540767	T2	20021203	JP 2000-599385	20000210
	US 6531506	B1	20030311	US 2000-721261	20001121
PRAI	US 1996-23397P	P	19960813		
	US 1997-909523	A2	19970812		
	US 1999-252148	A	19990218		
	WO 2000-US3495	W	20000210		
OS	MARPAT 133:349972				
AB	R1R2XCOYR3R4 [I; X = C, O, N, S; Y = N, O, S; .gtoreq.1 of R1-R4 = H; R2 = H when X = N, R2 = null when X = S, O; R4 = H when Y = N, R4 = null when Y = S, O; R1, R3 = (substituted) alkyl, haloalkyl, cycloalkyl, aryl, acyl, heterocyclyl; and metabolites and degrdn. products thereof], were prepd. Thus, pentylamine in hexane was treated with octyl isocyanate followed by stirring and standing overnight to give 97% 1-octyl-3-pentylurea. The latter inhibited human sol. epoxide hydrolase with IC50 = 0.72 .mu.M. I may be used to purify, isolate, or inhibit epoxide hydrolase , and may be used in conjunction with herbicides, insecticides, and fungicides.				
ST	urea prepn soluble epoxide hydrolase inhibitor; thiocarbamate prepn soluble epoxide hydrolase inhibitor; antiinflammatory urea prepn; adult respiratory distress syndrome treatment urea				
IT	Respiratory distress syndrome (adult, treatment; prepn. of ureas and related compds. as sol. epoxide hydrolase inhibitors)				
IT	Fungicides (fungicides with epoxide hydrolase inhibitors; prepn. of ureas and related compds. as sol. epoxide hydrolase inhibitors)				
IT	Herbicides (herbicides with epoxide hydrolase inhibitors; prepn. of ureas and related compds. as sol. epoxide hydrolase inhibitors)				
IT	Insecticides (insecticides with epoxide hydrolase inhibitors; prepn. of ureas and related compds. as sol. epoxide hydrolase inhibitors)				
IT	Hormones, plant RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process) (plant growth regulators with epoxide hydrolase inhibitors; prepn. of ureas and related compds. as sol. epoxide hydrolase inhibitors)				
IT	Anti-inflammatory agents Antitumor agents (prepn. of ureas and related compds. as sol. epoxide hydrolase inhibitors)				
IT	9048-63-9, Epoxide hydrolase RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process) (inhibition, isolation, or purifn. of sol. epoxide hydrolase ; prepn. of ureas and related compds. as sol. epoxide hydrolase inhibitors)				
IT	1220-01-5P 246165-77-5P 306770-63-8P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic				

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

IT 538-75-0 621-08-9 1212-29-9 2016-57-1, 1-Decanamine
2158-10-3 2222-58-4 2387-23-7 3567-62-2 20258-07-5
31510-11-9 78829-17-1 86446-52-8 91990-71-5 148806-83-1
196791-88-5 246165-79-7 306770-64-9 306770-65-0 306770-66-1
306770-67-2 306770-68-3 306770-69-4 306770-70-7 306770-71-8
306770-72-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

IT 110-58-7, Pentylamine 1569-69-3, Cyclohexanethiol 3158-26-7, Octyl isocyanate 3173-53-3, Cyclohexyl isocyanate 5452-37-9, Cyclooctylamine

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 9048-63-9, **Epoxide hydrolase**

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)

(inhibition, isolation, or purifn. of sol. **epoxide hydrolase**; prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

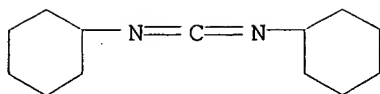
IT 538-75-0 2387-23-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

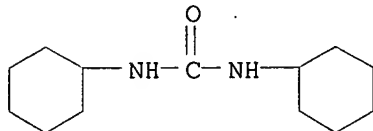
(prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

RN 538-75-0 HCAPLUS

CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)



RN 2387-23-7 HCAPLUS
 CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



L90 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2003 ACS
 AN 1999:503921 HCAPLUS
 DN 131:280999
 TI Potent urea and carbamate inhibitors of soluble **epoxide hydrolases**
 AU Morisseau, Christophe; Goodrow, Marvin H.; Dowdy, Deanna; Zheng, Jiang; Greene, Jessica F.; Sanborn, James R.; **Hammock, Bruce D.**
 CS Department of Entomology, University of California, Davis, CA, 95616, USA
 SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(16), 8849-8854
 CODEN: PNASA6; ISSN: 0027-8424
 PB National Academy of Sciences
 DT Journal
 LA English
 CC 1-3 (Pharmacology)
 Section cross-reference(s): 7, 25
 AB The sol. **epoxide hydrolase** (sEH) plays a significant role in the biosynthesis of inflammation mediators as well as xenobiotic transformations. Herein, the authors report the discovery of substituted ureas and carbamates as potent inhibitors of sEH. Some of these selective, competitive tight-binding inhibitors with nanomolar K_i values interacted stoichiometrically with the homogeneous recombinant murine and human sEHs. These inhibitors enhance cytotoxicity of trans-stilbene oxide, which is active as the epoxide, but reduce cytotoxicity of leukotoxin, which is activated by **epoxide hydrolase** to its toxic diol. They also reduce toxicity of leukotoxin in vivo in mice and prevent symptoms suggestive of acute respiratory distress syndrome. These potent inhibitors may be valuable tools for testing hypotheses of involvement of diol and epoxide lipids in chem. mediation in vitro or in vivo systems.
 ST **epoxide hydrolase** inhibitor urea carbamate structure
 IT Respiratory distress syndrome
 (adult, acute; potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)
 IT Lipids, biological studies
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (diol and epoxide; potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

- IT Structure-activity relationship.
(enzyme-inhibiting, **epoxide hydrolases**-inhibiting;
potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and
epoxide lipids and treatment of acute respiratory distress syndrome)
- IT Toxins
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
BSU (Biological study, unclassified); BIOL (Biological study); PROC
(Process)
(leukotoxins, cytotoxicity; potent urea and carbamate inhibitors of
sol. **epoxide hydrolases** in relation to structure
and role of diol and epoxide lipids and treatment of acute respiratory
distress syndrome)
- IT Enzyme kinetics
(of inhibition; potent urea and carbamate inhibitors of sol.
epoxide hydrolases in relation to structure and role
of diol and epoxide lipids and treatment of acute respiratory distress
syndrome)
- IT 1439-07-2, trans-Stilbene oxide
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
BSU (Biological study, unclassified); BIOL (Biological study); PROC
(Process)
(cytotoxicity; potent urea and carbamate inhibitors of sol.
epoxide hydrolases in relation to structure and role
of diol and epoxide lipids and treatment of acute respiratory distress
syndrome)
- IT 246165-79-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases**
in relation to structure and role of diol and
epoxide lipids and treatment of acute respiratory distress syndrome)
- IT 57-13-6, Urea, biological studies 64-10-8, N-Phenylurea
102-04-5 102-06-7, N,N'-Diphenylguanidine 102-09-0 538-75-0,
Dicyclohexylcarbodiimide 603-54-3 611-92-7 612-01-1
623-95-0, N,N'-Dipropylurea 722-01-0 1212-29-9, N,N'-
Dicyclohexylthiourea 2387-23-7, N,N'-**Dicyclohexylurea**
4559-87-9 13074-28-7 20258-07-5 31510-11-9 36102-06-4 82389-34-2
246165-77-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases**
in relation to structure and role of diol and
epoxide lipids and treatment of acute respiratory distress syndrome)
- IT 9048-63-9, **Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases**
in relation to structure and role of diol and
epoxide lipids and treatment of acute respiratory distress syndrome)
- IT 2038-57-5, Benzenepropanamine 3173-53-3, Cyclohexylisocyanate
RL: RCT (Reactant); RACT (Reactant or reagent)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases**
in relation to structure and role of diol and
epoxide lipids and treatment of acute respiratory distress syndrome)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 57-13-6, Urea, biological studies 538-75-0,

Dicyclohexylcarbodiimide 2387-23-7, N,N'-

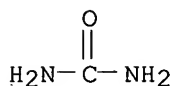
Dicyclohexylurea

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(potent urea and carbamate inhibitors of sol. epoxide hydrolases in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

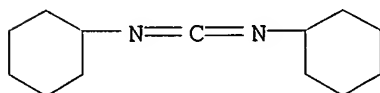
RN 57-13-6 HCAPLUS

CN Urea (8CI, 9CI) (CA INDEX NAME)



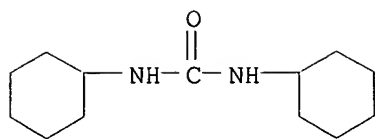
RN 538-75-0 HCAPLUS

CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)



RN 2387-23-7 HCAPLUS

CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



IT 9048-63-9, **Epoxide hydrolase**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 1998:554776 HCAPLUS

DN 129:256849

TI Mechanism of mammalian soluble **epoxide hydrolase** inhibition by **chalcone oxide** derivatives

AU Morisseau, Christophe; Du, Gehua; Newman, John W.; **Hammock, Bruce D.**

CS Department of Entomology and Department of Environmental Toxicology, University of California, Davis, CA, 95616, USA

SO Archives of Biochemistry and Biophysics (1998), 356(2), 214-228
CODEN: ABBIA4; ISSN: 0003-9861

PB Academic Press

DT Journal

LA English

CC 7-3 (Enzymes)

AB A series of substituted **chalcone oxides**

(1,3-diphenyl-2-oxiranyl propanones) and structural analogs was synthesized to investigate the mechanism by which they inhibit sol. **epoxide hydrolases** (sEH). The inhibitor potency and inhibition kinetics were evaluated using both murine and human recombinant sEH. Inhibition kinetics were well described by the kinetic models of A. R. Main (1982, in Introduction to Biochem. Toxicol., pp. 193-223, Elsevier, New York) supporting the formation of a covalent enzyme-inhibitor intermediate with a half-life inversely proportional to inhibitor potency. Structure-activity relationships describe active-site steric constraints and support a mechanism of inhibition consistent with the electronic stabilization of the covalent enzyme-inhibitor intermediate. The electronic effects induced by altering the ketone functionality and the para-substitution of the Ph attached to the epoxy C1 (i.e., the .alpha.-carbon) had the greatest influence on inhibitor potency. The direction of the obsd. influence was reversed for the inhibitory potency of glycidol (1-phenyl-2-oxiranylpropanol) derivs. Recent insights into the mechanism of **epoxide hydrolase** activity are combined with these exptl. results to support a proposed mechanism of sEH inhibition by **chalcone oxides**. (c)
1998 Academic Press.

ST **epoxide hydrolase** inhibition **chalcone oxide** prepn

IT Structure-activity relationship

(enzyme-inhibiting; mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)

IT QSAR (structure-activity relationship)

(mechanism of mammalian sol. **epoxide hydrolase**)

- inhibition by **chalcone oxide** derivs.)
- IT Enzyme kinetics
(of inhibition; mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)
- IT 5411-12-1 5633-36-3 6969-02-4 29425-81-8 32046-97-2
32047-01-1 32753-95-0 38860-42-3 40327-51-3 40327-54-6
40327-57-9 40327-58-0 42846-54-8 51477-11-3 55456-93-4
73354-53-7 93900-17-5 112711-73-6 131138-95-9 137487-67-3
147316-82-3 155190-86-6 203925-63-7 203925-65-9 213698-84-1
213698-85-2 213698-86-3 213698-87-4 213698-88-5 213698-89-6
213698-90-9 213698-91-0 213698-92-1 213698-93-2 213698-94-3
213698-95-4 213698-96-5 213698-97-6 213698-99-8 213699-01-5
213699-02-6 213699-04-8 213699-05-9 213699-06-0 213699-07-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)
- IT 9048-63-9, **Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)
- IT 203925-64-8P 213698-98-7P 213699-00-4P 213699-03-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of substituted **chalcone oxides** and structural analogs for investigating their mechanism of **epoxide hydrolase** inhibition)
- IT 67-36-7 98-86-2, reactions 2403-28-3, 4-
Phenylchalcone 4663-33-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant in prepn. of substituted **chalcone oxides** and structural analogs for investigating their mechanism of **epoxide hydrolase** inhibition)
- IT 13677-55-9P 213699-08-2P 213699-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reactant in prepn. of substituted **chalcone oxides** and structural analogs for investigating their mechanism of **epoxide hydrolase** inhibition)

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

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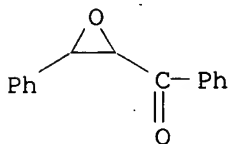
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IT 5411-12-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mechanism of mammalian sol. **epoxide hydrolase**
inhibition by **chalcone oxide** derivs.)

RN 5411-12-1 HCAPLUS

CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)



IT 9048-63-9, **Epoxide hydrolase**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mechanism of mammalian sol. **epoxide hydrolase**
inhibition by **chalcone oxide** derivs.)

RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

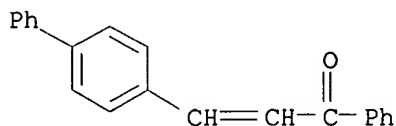
IT 2403-28-3, **4-Phenylchalcone**

RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant in prepn. of substituted **chalcone oxides**
and structural analogs for investigating their mechanism of
epoxide hydrolase inhibition)

RN 2403-28-3 HCAPLUS

CN 2-Propen-1-one, 3-[1,1'-biphenyl]-4-yl-1-phenyl- (9CI) (CA INDEX NAME)



L90 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 1998:123974 HCAPLUS

DN 128:201056

TI Methods of treating adult respiratory distress syndrome and other inflammatory diseases mediated by polyunsaturated lipid metabolites, and assays for **epoxide hydrolase** inhibitors

IN **Hammock, Bruce D.**; Moghaddam, Mehran F.; Cheek, Jeffrey M.; Borhan, Babak; Fergusson, James; Grant, David F.; Greene, Jessica F.; Matoba, Kazu; Zheng, Jiang; Sisemore, Marlene F.

PA Regents of the University of California, USA

SO PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A01N033-02

ICS A01N043-20; A01N043-24; A01N037-02; A61K031-13; A61K031-23; A61K031-335

CC 1-7 (Pharmacology)

Section cross-reference(s): 7

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9806261	A1	19980219	WO 1997-US14385	19970813
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5955496	A	19990921	US 1997-909523	19970812
	AU 9740692	A1	19980306	AU 1997-40692	19970813
	EP 926951	A1	19990707	EP 1997-938335	19970813
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	US 6174695	B1	20010116	US 1999-312207	19990514
PRAI	US 1996-23397P	P	19960813		
	US 1997-909523	A	19970812		
	WO 1997-US14385	W	19970813		

AB Methods are provided for treating inflammatory diseases mediated by polyunsatd. lipid metabolites by inhibiting **epoxide hydrolase**. The methods may be used for treating e.g. adult respiratory distress syndrome. Also provided are methods for assaying or screening the **epoxide hydrolase** inhibitors for inhibitory specificity and for toxicity, as well as novel biol. active THF diols of arachidonic acid, including antibodies thereto.

ST inflammatory disease treatment **epoxide hydrolase**

inhibitor; polyunsatd lipid metabolite inflammatory disease; screening.
epoxide hydrolase inhibitor inflammation; ARDS
epoxide hydrolase inhibitor

- IT Respiratory distress syndrome
 - (adult; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Lipids, biological studies
 - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (alkoxides; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Lung
 - (alveolus, epithelium, cells; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Nucleic acids
 - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (antisense; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Insect (Insecta)
 - (cell line; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Lipids, biological studies
 - RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 - (dihydroxy-; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Imides
 - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (diimides, lipophilic; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Immunoassay
 - (enzyme-linked immunosorbent assay; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Animal tissue culture
 - Anti-inflammatory agents
 - Biological transport
 - Drug screening
 - Spodoptera frugiperda
 - Structure-activity relationship
 - (**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Biological transport
 - (influx, calcium; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Baculoviridae
 - (insect cell line transfected with; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other

- inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Skin
(keratinocyte; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Toxins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(leukotoxins, metabolites; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT Antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(to arachidonate THF diol metabolites; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT 6088-36-4, Methyl isoleukotoxin diol 73889-55-1, Isoleukotoxin diol 189191-41-1, Leukotoxin diol 189191-42-2, Methyl leukotoxin diol
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT 112-63-0, Methyl linoleate 10547-36-1, Methyl isoleukotoxin 21019-43-2, Methyl leukotoxin 126639-26-7, Isoleukotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT 112-63-0D, Methyl linoleate, diepoxides 538-75-0, Dicyclohexylcarbodiimide 1885-07-0D, derivs. 5411-12-1 5411-12-1D, Chalcone oxide, derivs. 5633-36-3 6969-02-4 29425-81-8 32046-97-2 32753-95-0 40327-51-3 40327-54-6 40327-57-9 40327-58-0 42846-54-8 51477-11-3 203925-63-7 203925-64-8 203925-65-9 203925-66-0 203925-67-1 203925-68-2 203925-69-3 203925-70-6 203925-71-7 203925-72-8 203925-73-9 203925-74-0 203925-75-1 203925-76-2 203925-77-3 203925-78-4 203925-79-5 203925-80-8 203925-81-9 203925-82-0 203925-83-1 203925-84-2 203925-85-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT 9048-63-9, **Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT 506-32-1D, Arachidonic acid, THF diols
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
- IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(intracellular; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT 506-32-1, Arachidonic acid

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(metabolites; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) D'Amato; US 5503990 A 1997 HCAPLUS

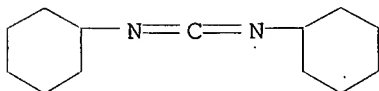
IT 538-75-0, Dicyclohexylcarbodiimide 1885-07-0D, derivs. 5411-12-1 5411-12-1D, Chalcone oxide, derivs.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

RN 538-75-0 HCAPLUS

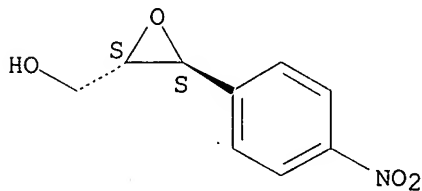
CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)



RN 1885-07-0 HCAPLUS

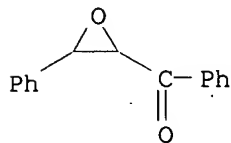
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



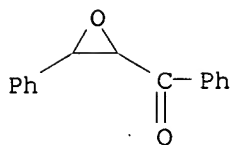
RN 5411-12-1 HCAPLUS

CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)



RN 5411-12-1 HCAPLUS

CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)

IT 9048-63-9, **Epoxide hydrolase**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 1993:443970 HCAPLUS

DN 119:43970

TI The interaction of cytosolic **epoxide hydrolase** with chiral epoxides

AU Dietze, Eric C.; Kuwano, Eiichi; **Hammock, Bruce D.**

CS Dep. Entomol., Univ. California, Davis, CA, 95616, USA

SO International Journal of Biochemistry (1993), 25(1), 43-52

CODEN: IJBOBV; ISSN: 0020-711X

DT Journal

LA English

CC 7-3 (Enzymes)

AB The kinetic parameters of the cytosolic **epoxide hydrolase** were examd. with two sets of spectrophotometric substrates. The (2S, 3S)- and (2R, 3R)-enantiomers of 4-nitrophenyl trans-2,3-epoxy-3-phenylpropyl carbonate had a KM of 33 and 68 .mu.m and a Vmax of 16 and 27 .mu.mol/min/mg, resp. With the (2S,3S)- and (2R,3R)-enantiomers of 4-nitrophenyl trans-2,3-epoxy-3-(4-nitrophenyl)propyl carbonate, cytosolic **epoxide hydrolase** had a KM of 8.0 and 15 .mu.M and a Vmax of 7.8 and 5.0 .mu.mol/min/mg, resp. Glycidyl 4-nitrobenzoate had the lowest I50 of the compds. tested in the glycidyl 4-nitrobenzoate series (I50 = 140 .mu.M). The I50 of the (2R)-enantiomer was 3.7-fold higher. The inhibitor with the lowest I50 in the glycidol series, and the lowest I50 of any compd. tested, was (2S,3S)-3-(4-nitrophenyl)glycidol (I50 = 13.0 .mu.M). It also showed the greatest difference in I50 between the enantiomers (330-fold). All enantiomers of glycidyl 4-nitrobenzoates and trans-3-phenylglycidols gave differential inhibition of cytosolic **epoxide hydrolase**. However, neither the (S,S)-/(S)- or (R,R)-/(R)-enantiomer always had the lower I50. Addn. of one or more Me groups to either enantiomer of glycidyl 4-nitrobenzoate resulted in increased I50. However, addn. of a Me group to C2 of either enantiomer of 3-phenylglycidol resulted in a decreased I50. Finally, when the hydroxyl group of trans-3-(4-nitrophenyl)glycidol was esterified the I50 of the (2S,3S)- but not the (2R,3R)-enantiomer increased.

ST cytosol **epoxide hydrolase** stereochem; enantiomer glycidyl nitrobenzoate phenylglycidol **epoxide hydrolase**

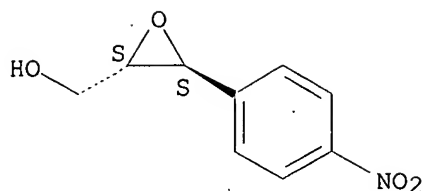
IT Stereochemistry
(of **epoxide hydrolase** reaction with glycidyl nitrobenzoates and Ph glycidols and epoxy carbonates)

IT Michaelis constant
(of **epoxide hydrolase**, of cytosol)

IT Kinetics, enzymic

- (of inhibition, of cytosolic **epoxide hydrolase** by glycidyl nitrobenzoate and Ph glycidol enantiomers)
- IT Cytoplasm
(cytosol, **epoxide hydrolase** of, chiral epoxides reaction with and inhibition of)
- IT Molecular structure-biological activity relationship
(**epoxide hydratase**-inhibiting, of glycidyl nitrobenzoate and Ph glycidol enantiomers)
- IT Isomerism and Isomers
(optical, of glycidyl nitrobenzoates and Ph glycidols and epoxy carbonates, cytosolic **epoxide hydrolase** interaction with)
- IT **9048-63-9, Epoxide hydrolase**
RL: PROC (Process)
(chiral epoxides reaction with and inhibition of, of cytosol)
- IT 106268-95-5 106268-96-6 106268-97-7 106268-98-8 106948-05-4
107033-44-3 115362-13-5 115459-65-9 118200-96-7 130550-48-0
141700-91-6 141782-32-3
RL: BIOL (Biological study)
(cytosolic **epoxide hydrolase** inhibition by, structure in relation to)
- IT 137461-28-0P 137461-29-1P 137493-99-3P 137494-00-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cytosolic **epoxide hydrolase** inhibition by, structure in relation to)
- IT 147349-28-8P 147349-29-9P 147385-51-1P 147385-52-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cytosolic **epoxide hydrolase** reaction with)
- IT 7693-46-1, 4-Nitrophenyl chloroformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Ph glycidol and **nitrophenyl glycidol** enantiomers)
- IT 98-88-4, Benzoyl chloride 108-24-7, Acetic anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with **nitrophenyl glycidol** enantiomers)
- IT **1885-07-0 37141-32-5**
RL: BIOL (Biological study)
(reaction with nitrophenyl chloroformate and acetic anhydride and benzoyl chloride and cytosolic **epoxide hydrolase** inhibition by)
- IT 98819-68-2 104196-23-8, (2S,3S)-3-Phenylglycidol
RL: BIOL (Biological study)
(reaction with nitrophenyl chloroformate and cytosolic **epoxide hydrolase** inhibition by)
- IT **9048-63-9, Epoxide hydrolase**
RL: PROC (Process)
(chiral epoxides reaction with and inhibition of, of cytosol)
- RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)
- *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
- IT **1885-07-0 37141-32-5**
RL: BIOL (Biological study)
(reaction with nitrophenyl chloroformate and acetic anhydride and benzoyl chloride and cytosolic **epoxide hydrolase** inhibition by)
- RN 1885-07-0 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

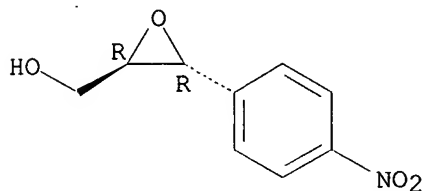
Absolute stereochemistry.



RN 37141-32-5 HCAPLUS

CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L90 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 1993:208242 HCAPLUS

DN 118:208242

TI Inhibition of **epoxide hydrolase** from human, monkey, bovine, rabbit and murine liver by trans-3-phenylglycidols

AU Dietze, Eric C.; Casas, Josefna; Kuwano, Eiichi; **Hammock, Bruce D.**

CS Dep. Entomol. Environ. Toxicol., Univ. California, Davis, CA, 95616, USA

SO Comparative Biochemistry and Physiology, Part B: Biochemistry & Molecular Biology (1993), 104B(2), 309-14

CODEN: CBPBB8; ISSN: 0305-0491

DT Journal

LA English

CC 7-3 (Enzymes)

Section cross-reference(s): 13

AB trans-3-Phenylglycidols were potent inhibitors of cytosolic **epoxide hydrolases** in all species tested. The order of inhibitor potency varied from species to species but trans-3-(4-nitrophenyl)glycidols were always the most potent inhibitors tested for cytosolic **epoxide hydrolase**.

The S,S-enantiomer was a more potent cytosolic **epoxide hydrolase** inhibitor than the R,R-enantiomer when a free hydroxyl group was present. However, (2R,3R)-1-benzoyloxy-2,3-epoxy-3-(4-nitrophenyl)propane was always a better inhibitor than the (2S,3S)-enantiomer. All microsomal **epoxide hydrolases** were poorly inhibited by the trans-3-phenylglycidols, and related compds., tested: The best new microsomal **epoxide hydrolase** inhibitor tested was (1S,2S)-1-phenylpropylene oxide which gave 18-63% inhibition, at 2 mM, depending on the species tested.

ST mammal liver **epoxide hydrolase** inhibition
phenylglycidol

IT Microsome

(**epoxide hydrolase** of, of mammalian liver, phenylglycidols inhibition of, species differences in and structure in relation to)

IT Liver, composition

(**epoxide hydrolases** of cytosol and microsome of, of mammals, phenylglycidols inhibition of, species differences in and structure in relation to)

IT Cattle

Macaca mulatta

Mouse

Rabbit

(**epoxide hydrolases** of liver cytosol and microsome
of, phenylglycidols inhibition of, other mammals comparison with and
structure in relation to)

IT Mammal

(**epoxide hydrolases** of liver cytosol and microsome
of, phenylglycidols inhibition of, species differences in and structure
in relation to)

IT Cytoplasm

(cytosol, **epoxide hydrolase** of, of mammalian liver,
phenylglycidols inhibition of, species differences in and structure in
relation to)

IT Molecular structure-biological activity relationship

(**epoxide hydratase**-inhibiting, of phenylglycidols)

IT 1885-07-0 4518-66-5 14212-54-5 37141-32-5

98819-68-2 104196-23-8 137461-29-1 137494-00-9

RL: BIOL (Biological study)

(**epoxide hydrolases** of mammalian liver cytosol and
microsome inhibition by, species differences in and structure in
relation to)

IT 112711-73-6 137461-30-4 147316-82-3

RL: BIOL (Biological study)

(**epoxide hydrolases** of mammalian liver cytosol
inhibition by, species differences in and structure in relation to)

IT 286-20-4, Cyclohexene oxide

RL: BIOL (Biological study)

(**epoxide hydrolases** of mammalian liver microsome
inhibition by, species differences in and structure in relation to)

IT 9048-63-9, Epoxide hydrolase

RL: BIOL (Biological study)

(inhibition of cytosolic and microsomal, of mammalian liver by
phenylglycidols, species differences in and structure in relation to)

IT 1885-07-0 37141-32-5

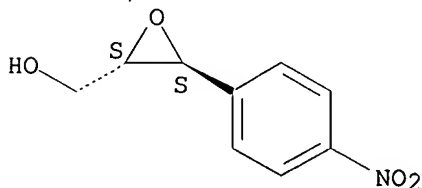
RL: BIOL (Biological study)

(**epoxide hydrolases** of mammalian liver cytosol and
microsome inhibition by, species differences in and structure in
relation to)

RN 1885-07-0 HCAPLUS

CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

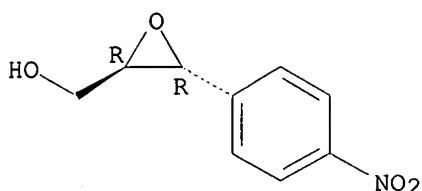
Absolute stereochemistry.



RN 37141-32-5 HCAPLUS

CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 9048-63-9, Epoxide hydrolase

RL: BIOL (Biological study)

(inhibition of cytosolic and microsomal, of mammalian liver by phenylglycidols, species differences in and structure in relation to)

RN 9048-63-9 HCAPLUS

CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2003 ACS

AN 1991:672840 HCAPLUS

DN 115:272840

TI Inhibition of cytosolic epoxide hydrolase by trans-3-phenylglycidols

AU Dietze, Eric C.; Kuwano, Eiichi; Casas, Josefina; Hammock, Bruce D.

CS Dep. Entomol., Univ. California, Davis, CA, 95616, USA

SO Biochemical Pharmacology (1991), 42(6), 1163-75

CODEN: BCPCA6; ISSN: 0006-2952

DT Journal

LA English

CC 4-3 (Toxicology)

Section cross-reference(s): 27

AB The inhibition of murine cytosolic epoxide hydrolase

was studied with both racemic and enantiomerically pure

trans-3-phenylglycidols. These compds. are the first enantioselective, slow binding inhibitors of cytosolic epoxide hydrolase

. The (2S,3S)-3-phenylglycidol enantiomer was always a better inhibitor than the (2R,3R)-enantiomer. When the I50 values of (2S,3S)- and (2R,3R)-3-(4-nitrophenyl)glycidol were

compared, the (2S,3S)-enantiomer was at least a 750-fold better inhibitor (I50 = 1.6 .mu.M) than the (2R,3R)-enantiomer (I50 = 1200 .mu.M), and it

was the most potent inhibitor tested in the 3-phenylglycidol series. If the hydroxyl group of the glycidol was masked or converted to another functionality, the potency of the inhibitor decreased and the

(2S,3S)-enantiomer was not necessarily the better inhibitor. In addn.,

trans-3-phenylglycidols demonstrated slow binding inhibition of cytosolic epoxide hydrolase. Inhibitors without a hydroxyl group,

or with a blocked hydroxyl group, were not slow binding inhibitors. These results suggested that the hydroxyl group was important in both

enantioselectivity and time dependence of inhibition of cytosolic

epoxide hydrolase by trans-3-phenylglycidols. The

hydration pattern of (2S,3S)- and (2R,3R)-2,3-epoxy-3-(4-nitrophenyl)glycidol by cytosolic epoxide

hydrolase also differed. When incorporation of [18O] from water

catalyzed by cytosolic epoxide hydrolase was measured,

the (2S,3S)-enantiomer gave 12% incorporation into the benzylic carbon and

the (2R,3R)-enantiomer gave 40% incorporation into the benzylic carbon.

Finally, trans-3-phenylglycidols were poor inhibitors of microsomal

epoxide hydrolase.

ST phenylglycidol epoxide hydrolase cytosol

IT Liver, composition

(epoxide hydrolase of cytosol and microsomes of, phenylglycidols effect on)

IT Microsome
(**epoxide hydrolase** of liver, phenylglycidols effect on)

IT Cytoplasm
(cytosol, **epoxide hydrolase** of liver, phenylglycidols effect on)

IT Molecular structure-biological activity relationship
(**epoxide hydratase**-inhibiting, by phenylglycidols, in liver cytosol and microsomes)

IT 1885-07-0 4518-66-5 14212-54-5 37141-32-5
98819-68-2 104196-23-8 106948-05-4 115362-13-5
RL: BIOL (Biological study)
(**epoxide hydrolase** of liver cytosol response to)

IT 9048-63-9, **Epoxide hydrolase**
RL: BIOL (Biological study)
(of liver cytosol and microsomes, phenylglycidols effect on)

IT 137461-26-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and oxidn. of)

IT 38860-42-3P 112711-73-6P 137461-27-9P 137461-28-0P 137461-29-1P
137487-67-3P 137493-99-3P 137494-00-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and **epoxide hydrolase** of liver cytosol response to)

IT 555-16-8, 4-Nitrobenzaldehyde, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydroxypropyltriphenylphosphonium bromide)

IT 51860-45-8, 3-Hydroxypropyltriphenylphosphonium bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with nitrobenzaldehyde)

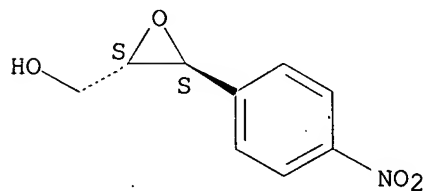
IT 5411-12-1, **Chalcone oxide** 137461-30-4
137494-01-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(redn. of)

IT 1885-07-0 37141-32-5
RL: BIOL (Biological study)
(**epoxide hydrolase** of liver cytosol response to)

RN 1885-07-0 HCAPLUS

CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

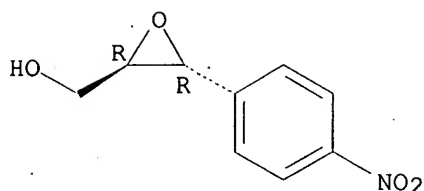
Absolute stereochemistry.



RN 37141-32-5 HCAPLUS

CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

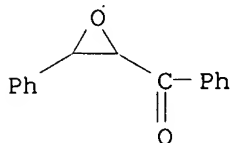
Absolute stereochemistry.



IT 9048-63-9, **Epoxide hydrolase**
 RL: BIOL (Biological study)
 (of liver cytosol and microsomes, phenylglycidols effect on)
 RN 9048-63-9 HCAPLUS
 CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 5411-12-1, **Chalcone oxide**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (redn. of)
 RN 5411-12-1 HCAPLUS
 CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)



=> d all tot hitstr

L98 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
 AN 2002:290322 HCAPLUS
 TI Inhibitors of soluble **epoxide hydrolase** attenuate
vascular smooth muscle cell
proliferation
 AU Davis, Benjamin B.; Thompson, David A.; Howard, Laura L.; Morisseau,
 Christophe; **Hammock, Bruce D.; Weiss, Robert H.**
 CS Division of Nephrology, Department of Internal Medicine, Cell and
 Developmental Biology Graduate Group, University of California, Davis, CA,
 95616, USA
 SO Proceedings of the National Academy of Sciences of the United States of
 America (2002), 99(7), 4752
 CODEN: PNASA6; ISSN: 0027-8424
 PB National Academy of Sciences
 DT Journal; Errata
 LA English
 AB Unavailable

L98 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
 AN 1999:12816 HCAPLUS
 DN 130:163515
 TI 14,15-**Epoxyeicosatrienoic acid** inhibits prostaglandin E2
 production in **vascular smooth muscle**
cells
 AU Fang, Xiang; Moore, Steven A.; Stoll, Lynn L.; Rich, Gretchen; Kaduce,
 Terry L.; Weintraub, Neal L.; Spector, Arthur A.
 CS Departments of Biochemistry, University of Iowa, Iowa City, IA, 52242, USA
 SO American Journal of Physiology (1998), 275(6, Pt. 2), H2113-H2121

CODEN: AJPHAP; ISSN: 0002-9513

PB American Physiological Society

DT Journal

LA English

CC 2-9 (Mammalian Hormones)

AB 4,15-**Epoxyeicosatrienoic** acid (EET), a cytochrome P 450 epoxygenase product of arachidonic acid (AA), reduced PGE2 formation by 40-75% in porcine aortic and murine brain microvascular smooth muscle cells. The inhibition was reversed 6-10 h after removal of 14,15-EET from the medium and was regioisomeric specific; 8,9-EET produced a smaller effect, whereas 11,12- and 5,6-EET were ineffective. Although the cells converted 14,15-EET to 14,15-dihydroxyeicosatrienoic acid (14,15-DHET), 14,15-DHET did not inhibit PGE2 formation, and the 14,15-EET-induced inhibition was potentiated by 4-**phenylchalcone oxide**, an **epoxide hydrolase** inhibitor. The inhibition occurred when substrate amts. of arachidonic acid (AA) were used and was not accompanied by enhanced prodn. of other prostaglandins, suggesting an effect on PGH synthase; however, in murine cells, 14,15-EET did not reduce PGH synthase mRNA or protein. Moreover, the 14,15-EET-induced decrease in PGE2 prodn. was overcome by increasing the concn. of AA, but not oleic acid (which is not a substrate for PGH synthase). These findings suggest that 14,15-EET competitively inhibits PGH synthase activity in **vascular smooth muscle cells**. The 14,15-EET-induced inhibition of PGE2 prodn. resulted in potentiation of platelet-derived growth factor-induced smooth muscle cell proliferation, suggesting that the competitive inhibition of PGH synthase by 14,15-EET can affect growth responses in smooth muscle cells.

ST **epoxyeicosatrienoate** PGE2 **vascular smooth muscle**

IT Artery

(aorta; **epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in **vascular smooth muscle cells**)

IT Cell proliferation

(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. and potentiation of PDGF-induced proliferation in **vascular smooth muscle cells** and mechanism therefor)

IT Platelet-derived growth factors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. and potentiation of PDGF-induced proliferation in **vascular smooth muscle cells** and mechanism therefor)

IT Brain

(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in brain microvascular smooth muscle cells)

IT Blood vessel

(microvessel; **epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in brain microvascular smooth muscle cells)

IT Blood vessel

(**smooth muscle**; **epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in **vascular smooth muscle cells**)

IT 506-32-1, Arachidonic acid 81246-85-7 81276-03-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in **vascular smooth muscle cells**)

IT 79551-81-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in

- vascular smooth muscle cells)**
- IT 363-24-6, Prostaglandin E2
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(epoxyeicosatrienoic acid inhibition of PGE2 prodn. in vascular smooth muscle cells)
- IT 39391-18-9, PGH synthase
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(epoxyeicosatrienoic acid inhibition of PGE2 prodn. in vascular smooth muscle cells and mechanism therefor)

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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=> d his

(FILE 'HOME' ENTERED AT 16:40:10 ON 05 MAY 2003)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 16:40:20 ON 05 MAY 2003

E EPOXIDE HYDROLASE/CN

L1 1 S E3
SEL CHEM

FILE 'HCAPLUS' ENTERED AT 16:40:36 ON 05 MAY 2003

L2 2196 S L1
L3 2861 S E1-E12
L4 2861 S L2,L3
E WEISS R/AU
L5 372 S E3,E10
E WEISS ROB/AU
L6 183 S E4,E15
E HAMMOCK B/AU
L7 542 S E3-E7
L8 153 S L4 AND L5-L7
L9 13 S CIS() (EPOXYEICOSATRIEN? OR EPOXY EICOSATRIEN?)
L10 478 S EPOXYEICOSATRIEN? OR EPOXY EICOSATRIEN?
L11 11 S L5-L7 AND L9,L10
L12 11 S L8 AND L11
L13 11 S NITROPHENYLGLYCIDOL OR NITROPHENYL GLYCIDOL OR NITRO() (PHENYL
L14 9 S 4() (NITROPHENYLGLYCIDOL OR NITROPHENYL GLYCIDOL OR NITRO() (PH
L15 75 S CHALCONE OXIDE
L16 15 S (4 OR P OR PARA)() (PHENYLCHALCONE OXIDE OR PHENYL CHALCONE OX
L17 11 S (4 OR P OR PARA)() (FLUOROCHALCONE OXIDE OR FLUORO CHALCONE OX
L18 8782 S DICYCLOHEXYLCARBODIIMIDE OR DICYCLOHEXYL() (CARBODIIMIDE OR CAR
L19 25 S L5-L7 AND L13-L18
L20 23 S L19 AND L8
L21 0 S L19 AND L12.
L22 57 S (4 OR P OR PARA)() (PHENYLCHALCONE OR PHENYL CHALCONE OR FLUOR
L23 0 S ADAMANTYL DODECYL UREA
L24 0 S ADAMANT?(S) DODECYL?(S) UREA
L25 13 S CYCLOHEXYL(S) DODECYL(S) UREA
L26 0 S ADAMANT?(S) DODECYLUREA
L27 0 S CYCLOHEXYL(S) DODECYLUREA
L28 592 S DICYCLOHEXYLUREA OR DICYCLO HEXYL UREA OR DICYCLOHEXYL UREA O

FILE 'REGISTRY' ENTERED AT 16:57:12 ON 05 MAY 2003

E C23H44N2O2/MF

L29 1 S 2387-23-7
E 638.8.1/RID
L30 21 S E3 AND 3/NR AND DODECYL
L31 0 S L30 AND UREA
E C23H44N2O2/MF
L32 0 S E3 AND 638/RID
L34 1 S 5411-12-1
L35 1 S 2403-28-3
L36 1 S 1608-51-1
E C19H38N2O/MF
L37 5 S E3 AND 46.150.1/RID
L38 1 S L37 AND 1/NR
L39 328 S 638/RID AND 3/NR AND 2/N AND 1/O AND 1/NC
L40 66 S L39 AND UREA
L41 61 S L40 NOT S/ELS
L42 0 S L41 AND 23/C
L43 3 S L39 AND 23/C
L44 1 S 538-75-0
L45 2 S 1885-07-0 OR 37141-32-5
L46 19 S C9H9NO4/MF AND OC2/ES AND 46.150.18/RID AND 2/NR
L47 14 S L46 AND NITROPHENYL

L48 6 S L47 AND OXIRANEMETHANOL
L49 6 S L45,L48
L50 STR
L51 67542 S 638/RID
L52 50 S L50 SAM SUB=L51
L53 3291 S L50 FUL SUB=L51
L54 STR
L55 1 S L54 SAM SUB=L53
L56 STR L54
L57 1 S L56 SAM SUB=L53
L58 18 S L56 FUL SUB=L53
L59 13 S L58 AND 3/NR
L60 6 S L59 NOT ESTER
L61 5 S L60 AND 638.8/RID
SAV L61 KWON056/A

FILE 'HCAPLUS' ENTERED AT 17:21:45 ON 05 MAY 2003

L62 5 S L61

FILE 'REGISTRY' ENTERED AT 17:22:17 ON 05 MAY 2003

L63 1 S 402939-18-8

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L64 4 S L63
L65 339 S L29
L66 3258 S L44
L67 23 S L49
L68 155 S L34
L69 33 S L35
L70 68 S L36

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L71 1 S 97717-69-6
E C20H32O3/MF
L72 2227 S E3
L73 7 S L72 AND EICOSATRIENOIC
L74 1 S L73 AND EPOXY
L75 6 S L73 NOT L74

FILE 'HCAPLUS' ENTERED AT 17:26:09 ON 05 MAY 2003

L76 95 S L74
L77 3890 S L62,L64-L70,L76
L78 25 S L5-L7 AND L77
L79 22 S L78 AND L4
L80 17 S L79 AND L9-L28
L81 8 S L78,L79 NOT L80
SEL DN AN 1 3
L82 2 S E1-E6
SEL DN AN 1 3 4 7 8 11 12 13 15 16 L80
L83 10 S E7-E36
L84 12 S L82,L83 AND L77-L83
L85 13 S L80,L81 NOT L84
SEL DN AN 1 3 9
L86 3 S L85 AND E37-E45
L87 15 S L84,L86

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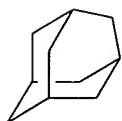
L88 1 S 57-13-6

FILE 'HCAPLUS' ENTERED AT 17:39:23 ON 05 MAY 2003

L89 2 S L88 AND L87
L90 15 S L87,L89
L91 33 S L4 AND L77

L92 18 S L91 NOT L87
L93 11294 S VASCULAR (S) SMOOTH (S) (MUSCLE OR MUSCULAR) (S) CELL
L94 18771 S VASCULAR (S) SMOOTH (S) (MUSCLE OR MUSCULAR)
L95 6 S L93,L94 AND L4
L96 4 S L95 NOT L87
SEL DN AN 3 4
L97 2 S L96 AND E46-E49
L98 2 S L97 AND L2-L28,L62,L64-L70,L76-L87,L89-L97
L99 1 S LIPID (S) ALKOXIDE AND L4
L100 32 S L4 AND L9,L10,L76
L101 7 S L4 AND L18,L66
L102 10 S L4 AND L13,L14,L67
L103 43 S L4 AND L15-L17,L68-L70
L104 7 S L100 AND L99,L101-L103
L105 5 S L104 NOT L87,L98
L106 8 S L103 AND L99-L102 NOT L87,L98
L107 8 S L105,L106
L108 55 S L99-L106 NOT L87,L98,L107

1 ANSWER 3642 OF 3648 REGISTRY COPYRIGHT 2003 ACS on STN
RN 281-23-2 REGISTRY
CN Tricyclo[3.3.1.1³,7]decane (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Adamantane (6CI, 8CI)
OTHER NAMES:
CN NSC 527913
FS 3D CONCORD
MF C10 H16
CI COM, RPS
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
CHEMINFORMRX, CHEMLIST, CIN, CSCHM, CSNB, DDFU, DETHERM*, DIPPR*,
DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*,
HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC,
PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(*Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2512 REFERENCES IN FILE CA (1937 TO DATE)
286 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2512 REFERENCES IN FILE CAPLUS (1937 TO DATE)
45 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L15 ANSWER 6 OF 18 USPATFULL on STN

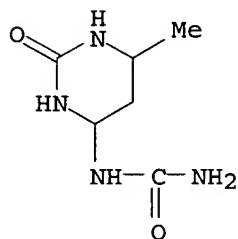
ACCESSION NUMBER: 87:45129 USPATFULL
TITLE: Anti-microbial compositions
INVENTOR(S): Fredrick, Jerome F., Bronx, NY, United States
PATENT ASSIGNEE(S): The Dodge Chemical Company, Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4675327		19870623
APPLICATION INFO.:	US 1983-483281		19830408 (6)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1977-786460, filed on 11 Apr 1977, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Robinson, Douglas W.		
LEGAL REPRESENTATIVE:	Conlin, David G., Williams, Gregory D.		
NUMBER OF CLAIMS:	13		
EXEMPLARY CLAIM:	1		
LINE COUNT:	340		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Embalming preparations, which are far less noxious than previously known compositions, comprise a combination of a disinfectant and a plant growth regulating compound. The compositions achieve anti-microbial potency at concentrations of these ingredients far lower than the concentration levels of disinfectants found in known embalming preparations.

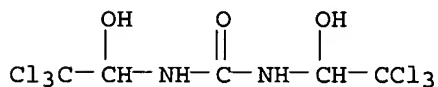
L8 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2003 ACS on STN
 RN 1129-42-6 REGISTRY
 CN Urea, (hexahydro-6-methyl-2-oxo-4-pyrimidinyl)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN (Hexahydro-6-methyl-2-oxo-4-pyrimidinyl)urea
 CN 2-Oxo-4-methyl-6-ureidohexahydropyrimidine
 CN **CDU**
 CN Crotodure
 CN Crotonylidenediurea
 CN Cyclo-Di-Urea
 CN Floranid
 CN Floranit
 CN Hexahydro-4-methyl-6-ureido-2-pyrimidone
 CN NSC 13403
 CN NSC 138171
 FS 3D CONCORD
 DR 12672-60-5, 37307-51-0
 MF C6 H12 N4 O2
 CI COM
 LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, IFICDB, IFIPAT, IFIUDB, NIOSHTIC, PROMT, TOXCENTER, USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: EINECS**, TSCA**
 (**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

127 REFERENCES IN FILE CA (1937 TO DATE)
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 127 REFERENCES IN FILE CAPLUS (1937 TO DATE)
 5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L9 ANSWER 25 OF 25 REGISTRY COPYRIGHT 2003 ACS on STN
 RN 116-52-9 REGISTRY
 CN Urea, N,N'-bis(2,2,2-trichloro-1-hydroxyethyl)- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Urea, 1,3-bis(2,2,2-trichloro-1-hydroxyethyl)- (6CI, 7CI, 8CI)
 OTHER NAMES:
 CN 1,3-Bis(1-hydroxy-2,2,2-trichloroethyl)urea
 CN 1,3-Bis(2,2,2-trichloro-1-hydroxyethyl)urea
 CN Crag Experimental Herbicide 2
 CN Crag Herbicide 2
 CN DCU
 CN Dichloral urea
 CN Dicloralurea
 CN DKhM
 CN EH2
 CN Experimental Herbicide 2
 CN NSC 32207
 CN RC 9485
 FS 3D CONCORD
 DR 12765-19-4
 MF C5 H6 Cl6 N2 O3
 CI COM
 LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, CA, CABA, CAOLD, CAPLUS,
 CASREACT, CHEMCATS, CHEMLIST, CIN, DDFU, DRUGU, HODOC*, HSDB*, IFICDB,
 IFIPAT, IFIUDB, MEDLINE, MSDS-OHS, NIOSHTIC, RTECS*, TOXCENTER, USAN,
 USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: EINECS**, WHO
 (**Enter CHEMLIST File for up-to-date regulatory information)



****PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT****

232 REFERENCES IN FILE CA (1937 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 233 REFERENCES IN FILE CAPLUS (1937 TO DATE)
 19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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L4 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:277838 CAPLUS

DOCUMENT NUMBER: 132:303489

TITLE: Method of treating immunological disorders mediated by t-lymphocytes

INVENTOR(S): Erickson, David; Grob, Peter M.; Hoffman, Ann F.; Warren, Thomas C.

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023060	A2	20000427	WO 1999-US24371	19991019
WO 2000023060	A3	20000908		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-104875P P 19981020

AB The use of **sol. epoxide hydrolase inhibitors** in the treatment of T-lymphocyte mediated immunol. disorders is described either as monotherapies or as part of combination therapies for such disorders. **Sol. epoxide hydrolase inhibitors** are e.g. N-[4-[5-ethyl-3-pyridin-3-yl-pyrazol-1-yl]-phenyl]nicotinamide.

6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 1994:498875 CAPLUS
DOCUMENT NUMBER: 121:98875
TITLE: Can we develop improved derivatives of valproic acid?
AUTHOR(S): Bialer, Meir; Haj-Yehia, Abdullah; Badir, Khalil;
Hadad, Salim
CORPORATE SOURCE: Fac. Med., Heb. Univ. Jerusalem, Jerusalem, 91120,
Israel
SOURCE: Pharmacy World & Science (1994), 16(1), 2-6
CODEN: PWSCED; ISSN: 0928-1231
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Valproic acid is one of the major antiepileptic drugs. A review with 35 refs. In animal models, valproate showed less anticonvulsant potency than the other three established antiepileptic drugs: phenobarbital, phenytoin and carbamazepine. In addn., two major side-effects, teratogenicity and hepatotoxicity, have been assocd. with valproate therapy. Due to the above and the shortage of new antiepileptic drugs there is a substantial need to develop improved derivs. of valproate. This paper analyzes three kinds of valproate derivs.: **valpromide**, the primary amide of valproate, and its analogs; monoester prodrugs of valproate and an active metabolite of valproate, 2-n-propyl-2-pentenoate. The comparative evaluation was carried out by pharmacokinetic and pharmacodynamic analyses in animals. From the data accumulated so far, the authors can conclude that 2-n-propyl-2-pentenoate and/or a **valpromide** isomer, which does not undergo amide-acid biotransformation and preferably is not an **epoxide hydrolase inhibitor**, may prove to be improved derivs. of the parent compd. valproic acid.

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:526069 CAPLUS
DOCUMENT NUMBER: 113:126069
TITLE: Unsubstituted amides: new class of potent inhibitors
of human microsomal epoxide hydrolase
AUTHOR(S): Kerr, Bradley M.; Levy, Rene H.
CORPORATE SOURCE: Sch. Pharm., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: Drug Metabolism and Disposition (1990), 18(4), 540-2
CODEN: DMDSAI; ISSN: 0090-9556
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Various lipophilic amides, including **valpromide** and progabide, were potent inhibitors of epoxide hydrolase in human liver microsomes. Possible drug interactions are discussed.